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BY A. B. MACALLUM.

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SURFACE TENSION AND VITAL PHENOMENA

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SURFACE TENSION AND VITAL PHENOMENA.

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I.—INTRODUCTION.

The investigations of the structure, composition and functions of animal and vegetable cells which have been made during the last eighty years have produced a body of knowledge which, considered from all points of view, is an imposing science and one that gives us a deep insight into the problems of the organic world. Its achievements in the way of widening our understanding of the processes of nature are far beyond what the workers in this field of fifty years ago dared to imagine as possible, and the result to-day is a worthy memorial of the intense enthusiasm of the scientific spirit which has been so extraordinary a factor in the progress of the last sixty years.

This body of knowledge, this lore of the organic world, is still, with all its achievements, an unsymmetrically developed science. Though all the interest of it ultimately lies in the problems it presents, it is chiefly, nay, almost wholly, concerned with the structural or morphological side of living matter, while of its functional phenomena our knowledge is only of the most general kind. The reason for this is not far to seek. What little we know of the functional side of the living cell, as, for example, of cellular secretion, absorption and nutrition, has only to a very limited extent been the outcome of observations directed to that end. It is indeed, in very great part, the result of all the inferences and generalizations drawn from the data of morphological research. The fact that it has been so obtained does not make it the less valuable or the less certain, but, simply because of its source and the method by which we have gained it, it is of a fragmentary character and, accordingly, less satisfactory in our estimation than if it were an achievement of direct observation.

This limitation of our knowledge has affected, or, to express it more explicitly, has fashioned our concept of living matter. When we think of the cell it is conceived as a morphological element almost exclusively. The functional aspect is not indeed ignored, but we know little about it, and we veil our ignorance by classing its manifestations as "vital phenomena".

Progress, indeed, there has been from the biochemical side in the last twenty years and more particularly in the last ten. We know much concerning ferment or catalytic action, and we have gained considerable knowledge concerning the physical and chemical properties of colloids. Further, we have obtained some insight into the constitution of proteins, and, in consequence, we are in a position to understand a little more clearly, though not fully, what happens in them when, on their decomposition in the cell, they produce the waste products, urea and other metabolites. Moreover, fats can be formed in the laboratory from glycerine and fatty acids, a large number of which have been synthesized, and a very large majority of the sugars of the aldohexose type have been built up from simpler compounds. Results like these indicate that some of the products of the activity of animal and vegetable cells may be paralleled in the laboratory, but that is as far as the resemblance extends. The methods of the laboratory are not yet those of nature. In the formation of carbohydrates the chlorophyll-holding cell makes use of processes of the most speedy and effective character, but nothing of these is known to us except that they are quite unlike the processes which the laboratory employs in the artificial synthesis of carbohydrates. Nature works unerringly, unfalteringly, with an amazing economy of material and energy, while "our laboratory syntheses are but roundabout ways to the sink".

In consequence, it is customary to regard living matter as unique, as a thing apart, without an analogue or parallel in the inorganic world, and the secrets involved in its actions and activities as insoluble enigmas. Influenced by this view, there are those who postulate, as an explanation for all these manifestations, the intervention, in so-called living matter, of a force otherwise and elsewhere unknown, biotic or vital, whose action is directed, according to the character of the structure through which it operates, to the production of the phenomena in question. Living matter is, from this point of view, but a mask and a medium for action of the unknown force.

This is the old doctrine of vitalism of the seventeenth and eighteenth centuries, and which still had many adherents in the first half of the nineteenth century. Its reassertion now in certain quarters in the scientific world is due to reaction from the enthusiasm born of the belief that the application of the known laws of physics and chemistry in the study of living matter would explain all its mysteries. From twenty to forty years ago hopes were high that the solution of these problems would result from a more profound comprehension of the laws of the physical world. Since then there has been an extraordinary increase in our knowledge of the structure and of the products of the activity of living matter without a corresponding increase in knowledge of the processes involved. The obscurity still involving the latter appears the more pronounced because of the high lights thrown on the former. Doubt, and even despair, has taken the place of hope with some, and the action of an unknown, mysterious force is invoked to explain what appears to them to be an insoluble enigma.

The persistence of the old doctrine of vitalism is, therefore, a reminder that our knowledge of the laws of matter, seemingly comprehensive, is not at present profound enough to enable us to solve all the problems involved in the vital phenomena. One cannot but admit, also, that our methods of investigation are very inadequate, a result very largely due to the fact that there has been a lack of investigators specially trained not only in biology, but also in physics and chemistry, for the very purpose of attacking intelligently these problems. The biologists, for want of such a wide training, have in their researches emphasized the morphological aspect and the readily observable phenomena of living matter. This situation has in recent years been accentuated by the high degree of specialism which certain departments of biology have developed. The physicist and chemist, on the other hand, knowing generally little of the morphology of the cell and of its vital manifestations, have been unable to apply satisfactorily the principles of their sciences in an explanation of the vital processes.

It must also be admitted that in some signal instances in which the physicist and chemist attempted to aid in the solution of biological problems the result has not been quite satisfactory. Especially has this been the result in the case of membranes. Arrhenius' theory of dissociation and van 't Hoff's gas theory of solutions were supported by such an array of facts from the side of physics and physical chemistry that there appeared to be no question whatever regarding their universal validity, and their application in the study of the phenomena of osmosis was urged with acclaim by physical chemists and eagerly welcomed by physiologists. The theories promised at first to explain all the processes involved in diffusion through membranes, but the final result was not in all cases what was expected. In illustration of this, one instance will suffice. The osmotic concentration of the blood in man as measured by the depression of the freezing point (Δ) ranges from −0.56 to −0.58°C. The concentration of the urine indicated in the same way is, except under rare conditions, always greater than this, and its value usually ranges between −1.50° and −3.00° C., that is, from more than two to five times that of the blood plasma. This result is the very opposite of that which should be expected from the application of the theories of Arrhenius and van 't Hoff.

It is, therefore, not surprising that there should be a reaction amongst physiologists and biologists, in some cases involving the extreme assumption that the laws of physics and chemistry are inadequate to explain the causation of vital phenomena. The assumption is, of course, not justifiable, for it postulates, among other things, that we fully comprehend now all the laws of the physical world. That the application of these laws has hitherto failed to explain the causation of vital phenomena does not prove that they are to be of no service in the solution of the problems involved. A more comprehensive examination of these will, it is reasonable to believe, lead to a quite different result.

The cause of the failure lies in our not fully applying all the principles involved in the theories of solution and the physics of fluids. One aspect of molecular physics was emphasized, while others of prime significance, as possible factors in the causation of the phenomena, were ignored or overlooked. Among these latter were surface tension, the intrinsic pressure of liquids, viscosity, and the thermodynamic relations of solutions, each of which plays a part in the functional manifestations of living matter.

How far each of these operates as a factor in these manifestations it is not yet safe to say. To attempt to estimate the force of each postulates a fuller knowledge of the scope of the operations of these factors than we possess. We are unable, as I shall show later, to determine definitely the intrinsic pressure in water, to say nothing of the physiological fluids. The thermodynamic relations of physiological fluids and of living matter constitute an almost unknown field to the physicist, as it does to the biologist. Only in surface tension are we in a position to ascertain whether there may be accord between theory and fact.

The time, therefore, appears ripe for a discussion of this principle as a factor in the manifestations of living matter. Further, my own observations on Microchemistry have turned my attention specially to it during the last eight years, and, as a consequence, the problems involved in Microchemistry have acquired, from this point of view, a special significance which, I believe, has not hitherto been discussed.

This explains the origin of the present contribution on the subject. About the views advanced here it suffices to say that they are offered with reserve. It is possible that I may have fallen into error, and I must, therefore, be prepared to recall or to revise some of the views which I have advanced should they ultimately be found wanting. That, I reassure myself, is the true attitude to take. It is a far cry to certainty. As Duclaux has aptly put it: "la science s'avance parcequ'elle n'est sure de rien". Thus I justify the attempt made in the following pages.

II.—SURFACE TENSION IN PURE FLUIDS AND SOLUTIONS.

The forces other than kinetic that are concerned in the equilibrium of pure fluids are all of molecular origin. The molecules are drawn to one another by a force which, it is postulated, varies inversely as the fourth power of the distance, and it is effective only at insensibly minute ranges. This attractive force tends, when the molecules come within effective range of each other, to reduce the space they occupy to the absolute minimum, in which case the fluid would become a dense solid. These molecules are also affected by a repulsive force arising from countless collisions due to the movement of the molecules amongst one another. This force is, unlike the attractive one, not an inherent property of the molecules, and is derived from without, usually through the accession of the energy we call heat. When this energy gives a high velocity to the molecules the fluid expands; the distance between the molecules is so increased that the attractive force is reduced to infinitely small value, and, in consequence, the matter forming the fluid is converted into the gaseous or vapour condition.

In a fluid, then, the molecules are still so near each other that each is under the influence of the attractive forces of the immediately adjacent molecules. By heating such a fluid in a closed space it will expand as a whole, till, at a certain temperature, the critical temperature, it reaches a condition, the critical condition, in which the fluid is on the point of transition from the fluid condition to the vapour condition. The volume of the fluid is now the critical volume, and in this condition each molecule is just so far apart from its immediate neighbours that the influence of the attractive force exerted is reduced to a minimum, in consequence of which the fluid tends to pass beyond the critical condition and become vapour.

The ratio of the critical volume to the normal volume is in a great majority of fluids very difficult, or impossible, to determine, and in only a very few of the remainder has it been directly ascertained. The values of the ratio so obtained are not concordant, as the results are affected by apparently large experimental errors. The theoretical value of the ratio has been developed from the equation of van der Waals:

$$\left(p + \frac{a}{v^2}\right)(v - b) = RT$$

in which b is 4 times the volume occupied by the molecules and $3b$ the critical volume. In the critical volume, if the latter were divided evenly between the molecules, each of these would occupy a cubical space whose volume could not exceed 12 times the volume of the molecule itself. As, however, the molecules are not spherical the space they occupy would be more than $\frac{b}{4}$, probably $\frac{b}{3}$, and, in consequence, the critical volume would be 9 times the attainable minimum volume.

From this it follows that the cubical space allotted to each molecule in the critical volume would have an edge $\sqrt[3]{9}$ times the diameter of the molecule, that is, the distance between the centres of two immediate adjacent molecules would not exceed $s\sqrt[3]{9}$, or a little more than twice the diameter (s) of a molecule. From this it follows that the diameter of the sphere of molecular attraction does not exceed twice the diameter of the molecule. The distance between the centres of two immediately adjacent molecules in a normal fluid, ordinarily, would, of course, be much less than twice the molecular diameter, and it is equal to that diameter when the molecules are in contact.*

The diameter of the molecules varies. According to Kelvin (61), the diameter of a molecule of hydrogen $= 1.81 \times 10^{-8}$cm., that of one of carbon dioxide $= 2.99 \times 10^{-8}$cm. In this case the diameter of the sphere of molecular attraction would with hydrogen be at most 3.6×10^{-8}cm., and with carbon dioxide 6×10^{-8}cm. Jäger (54) calculated the diameter of a molecule of chloroform to be about 8×10^{-7}cm. The maximum distance, therefore, through which the molecular attraction would be effective would be 16×10^{-7}cm. According to Drude (25), the thickness of the "black spot" in a glycerine soap film is 17×10^{-7} cm., but the thickness of the "black spot" in a soap film made with sodium oleate has, according to Johonott (60), a minimum of 6.2×10^{-7} cm. As this minimum is supposed to be at least twice the diameter of the molecules in the film the range of molecular attraction cannot exceed 6.2×10^{-7} cm., that is, the diameter of the sphere of molecular attraction is more than ten times that of carbon dioxide and somewhat less than that of chloroform. The diameter of the molecules of water vapour, as calculated from the oscillation experiments of Kundt and Warburg (63), is 3.39×10^{-8} cm.* This would make the diameter of the sphere of molecular attraction 7.78×10^{-8} cm. By employing a new method devised by himself, Garver (40) has recently calculated that the molecular range of action of water is 2.92×10^{-8} cm.

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* On the subject of the critical volume, the distance of the molecules from one another, and on the attractive force between them, *vide* Boynton, Applications of the Kinetic Theory to Gases, Vapors, Pure Liquids and the Theory of Solutions, New York, 1904; Jeans, The Dynamical Theory of Gases, Cambridge, 1904; Chwolson, Traité de Physique, Paris, 1911, Tome III., Chap. XIII.

The attraction between the molecules is the factor which produces in the interior of the fluid what is known as intrinsic pressure, and on the surface what is called surface tension.

The pressure due to the action of molecular attraction between the molecules in the interior of the fluid is, at the lowest estimate, an enormous one. This pressure is the value *K* of Laplace, represented by the integral

$$2\pi \int_0^b dz\,\psi(z)$$

and the term $\frac{a}{v^2}$ in the equation of van der Waals. Young (115) estimated it in water to be equivalent to 23,000 atmospheres, and Dupré (26), determining it from the mechanical equivalent of the latent heat of steam, placed it at 25,000 atmospheres, while van der Waals (111) gives the value as ranging between 10,500 and 10,700 atmospheres. Garver (40), however, estimates the intrinsic pressure in water to be 1,236 atmospheres.

The occurrence of this enormous pressure is difficult to conceive, but of its existence there can be no doubt. The impossibility of estimating it exactly is due to the fact that we have no means of determining directly the pressure exerted by the molecules on each other. All our values of pressure in a substance are obtained by finding what it exerts against an external substance, whereas we cannot take a single molecule and ascertain what pressure the molecules surrounding it exercise upon it.

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* *Vide* Jeans, The Dynamical Theory of Gases, 1904, p. 251.

On the surface of the fluid the molecular attraction manifests itself as surface tension. In the interior, within a certain distance of the surface, each molecule is affected in all directions equally by the molecular forces exerted by the surrounding molecules. The molecules of the superficial layer, on the other hand, providing they are not in contact with the molecules of a gas or of another fluid or of a solid, are affected only by their own forces and by those of the molecules below them. The attractive force they would exert externally is unengaged, that is, a certain amount of their energy is free, or in the potential condition. The amount of this free energy may be diminished by putting the superficial molecules in contact with those of a solid or of another fluid, and it is slightly diminished even by the molecules of the air or any other gas.

The superficial molecular layer thus forms an elastic membrane, the elastic character of which is due to the molecular forces between its molecules tending ever to bring them closer together, and yet at times subject to forces which may drive or draw them so far apart that their mutual attraction is ineffective and the elastic character disappears.

The attractive force between the molecules of the superficial layer would seem, from the correction term $\frac{a}{v^2}$ in van der Waals' equation, to vary inversely as the fourth power of the distance between them, and, consequently, as the molecules in the superficial layer are not as near one another as are those which lie deeper, the measure of the attractive force constituting the surface tension cannot be used as a factor in determining the intrinsic pressure.

Whatever, therefore, increases the distance between the molecules lessens not only the intrinsic pressure but also the surface tension, and, conversely, whatever decreases the distance increases the intrinsic pressure and the surface tension.

If the temperature of a fluid system is raised or lowered the kinetic energy of the molecules is increased or diminished, and thus the distance between the molecules is increased or diminished. An increase of the distance involves a decrease of surface tension, a decrease of the distance an increase of the surface tension. For the same reason the intrinsic pressure would be correspondingly altered.

It is possible, however, to affect the attraction between the superficial molecules without affecting the intrinsic pressure. This can be done by diminishing or increasing the electrical charge on the surface of a fluid system. That electrical charge is disposed in the form of two layers, one of which is situated in the most superficial molecules of the system (e.g., a drop of mercury), the other in the immediate external layer of molecules of the surrounding medium (e.g., air, water, oil, etc.). The charges in these two layers are of opposite sign. In the case of the drop of mercury the charge of the superficial molecules is positive and the other negative, but in other fluid systems and with external media the opposite relation of the layers may obtain. These conditions illustrate the electrical double layer phenomena postulated in the Lippmann-Helmholtz Theory of surface electrification. Now, in every surface endowed with such electrical double layer the electrostatic force tends ever to an extension of the area of the surface, that is, to reduce the value of the surface tension. The reason for this is that the electrical particles of the same sign, on or in the molecules, tend to repel one another, and this mutual repulsion opposes the attractive force between molecules of the superficial layer which carries the charge. If, now, at any point on the surface the originally present charge is increased through polarising forces, the repulsive effect of the charge is increased, and there results an increase of distance between the molecules and, in consequence, a decrease of surface tension, while a decrease of the charge brought about in the same way results in an increase of surface tension. The latter, however, does not, at its maximum, exceed that which the superficial layer of molecules would have in the complete absence of any charge or double layer.

Any charge, therefore, whether positive or negative, that the molecules of a superficial layer of a fluid system may have will diminish the attractive force between the individual molecules, and thus the surface tension in such a system is always less than that in a system in which no charge or double layer obtains.

The surface tension can be affected in a fluid system by its solutes. These, with exceptions, raise or lower surface tension. As a rule, the inorganic solutes raise it while the organic lower it, but not in proportion to concentration. Thus, in a solution of sodium chloride in water at 18° C. and at $\frac{1}{\infty}$ gram molecular concentration the surface tension is 75.3 dynes, but in 6.96 gram molecular concentration it is 85.04 (Gradenwitz, 43, and Volkmann, 110), while in a solution of butyric acid in water at 25°C. and at $\frac{1}{\infty}$ concentration the surface tension is 74.2 dynes, and at 2.834 gram molecular concentration it is 29.4 (Drucker, 24, and Freundlich, 36). The presence of organic substances in weak concentration in water thus greatly lessens surface tension, while a weak concentration of an inorganic substance, or even a great concentration, if it increases surface tension, only does so slightly.

The explanation for the capacity on the part of a solute to increase or decrease surface tension is not fully understood. To say that the solute increases or decreases the attraction between the molecules of the solvent is only another way of stating the fact without explaining it. It is to be noted, however, that those substances which in a fluid state have themselves a surface tension lower than that of their solvent (e.g., water), when dissolved in it lower its surface tension. Thus, liquid hydrochloric acid, liquid hydrobromic acid, liquid ammonia, and the organic fluids, benzol, methyl alcohol, ethyl alcohol, ether, chloroform, glycerol, acetone, pyridin, anilin, phenol and the organic acids, have of themselves a low surface tension and, when dissolved in water, decrease its tension, while the inorganic salts and the fixed alkalies which possess, when fused, a surface tension higher than that of water, and such an acid as sulphuric, which also has a surface tension higher than that of water, have the opposite effect on water on solution in it. Compounds formed between those that lower and those that raise the surface tension of water occupy an intermediate position. The organic acids, and especially the lower fatty acids and the oxyacids, have a marked effect in lowering the surface tension, but when they are combined with an inorganic base they only slightly affect the surface tension of water, mostly in the direction of lowering it. Acetic acid in a 1 per cent. concentration lowers the surface tension of water from 75 dynes to 63 (Traube, 108), while sodium acetate in the same concentration does not at all decrease the surface tension of the solution (Forch, 35). This is quite as marked in the case of butyric acid, which in a 1 per cent. solution lowers the surface tension of water from 75 dynes to 34.9 (Traube, 108), but a 0.9 per cent. aqueous solution of sodium butyrate has a surface tension of 70 dynes (Forch, 35).

The solutes that alter the surface tension of the solvent must affect the intrinsic pressure in the same. This would follow from the fact that a diminution or an increase of surface tension is fundamentally a decrease or an increase of molecular attraction. Therefore, when a solute raises or lowers surface tension it raises or lowers the intrinsic pressure, not, however, in the same proportion as it affects surface tension. On the other hand, for pure fluids the surface tension is an indication of the intrinsic pressure. If, for example, we knew the surface tension of two different pure fluids at a certain temperature and the intrinsic pressure of one of them, we might determine approximately the surface tension of the other. As already pointed out, however, in no case have we as yet determined even approximately the intrinsic pressure.

The effects exercised by the solutes on surface tension and intrinsic pressure cannot be proportional. If they were, then the solutes would be uniformly distributed throughout a fluid system. Now, in a fluid drop surrounded by air a solute that lowers the surface tension is more concentrated in the surface layer than elsewhere in the drop, while a solute that raises the surface tension is least concentrated in the surface layer of the system. This distribution of a solute in a fluid, whether it lowers or raises surface tension, is due to the action of a principle or law which may be expressed in words to the effect that the concentration throughout a fluid system tends to be so adjusted as to reduce the energy at every and any point in it to a minimum. The inequality in distribution of the solute indicates very clearly that the surface energy and intrinsic pressure are unequally affected by the solute, and, in consequence, the solute is concentrated where the energy of the pure solvent has been diminished, with the result that the energy per unit volume tends to be the same as elsewhere in the system.

The first to call attention to this phenomenon was J. Willard Gibbs (42), but in a form of statement whose significance was only later fully apprehended.* Eight years later, that is, in 1886, J. J. Thomson (102) independently discovered the principle involved, and in publishing his discovery in the following two years gave it concrete expression and added illustrations of its action. In consequence of these two sources of our knowledge of it, it is known as the Gibbs-Thomson principle, and it will be referred to hereafter in this contribution under that term.

Gibbs formulated the factors which would enable the concentration of the solute at the surface of a fluid system to be determined. These have been evaluated on the basis of the gas law, $P = RTC$, and the formula

$$\Gamma = -\frac{C}{RT} \cdot \frac{d\sigma}{dC}$$

has been obtained which permits us to calculate from ascertainable data what the concentration at the surface of a fluid system may be. In this formula Γ is the weight of the solute positively or negatively absorbed per cm.^{2} of the surface in excess of that which would have been at the surface in the absence of any adsorption; C, the concentration of the solute in the fluid; σ, the surface tension in dynes; R, the gas constant

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* Op. cit., pp. 380-393.

$$\left(=\frac{2 \times 4.2 \times 10^7 \text{ ergs}}{\text{molecular weight of solute}}\right),$$

and T = the absolute temperature.

Forch (35) was the first to provide data for the calculation of the concentration of an inorganic solute in the surface layer of a fluid system. In a normal solution of sodium chloride the diminution of the salt in the surface layer was estimated to be 0.024 mgm. per square metre. In the case of acetic acid which lowers the surface tension of water, and some of which, therefore, must be concentrated at the surface of the system, Whatmough (112) obtained results with a normal solution by which it was estimated that the excess of concentration of the acetic acid at the surface was 0.2 mgrm. per square metre, or nearly ten times the deficit in normal salt solutions, and that this concentration at the surface alters by less than 15 per cent., even when the concentration throughout the system was increased eightfold. Milner (85), driving air through a sodium oleate solution and collecting the foam formed, found that for solutions averaging 0.00204 grm. mol. per litre the concentration in the foam gave values from which he estimated that the surface concentration of the sodium oleate was 0.4 mgm. per square metre in excess over that of the fluid generally. On the other hand, by using the data obtained by Reinold and Rücker (92) from the conductivity of films made from a solution of 1 part of sodium oleate in 60 of water, Milner calculated that the surface excess would be 2.4 mgm. per square metre.

These values are all very small, and were they the only ones accessible, surface concentration as a result of surface tension would, except for certain problems of very limited interest, be negligible. There are other experimentally obtained values which put the surface concentration in quite another light, and which must now be referred to.

Miss C. C. Benson (5), using an aqueous solution of amyl alcohol, in which the surface tension falls very rapidly with the increase of the concentration of the solute, and which also develops foam very easily, collected the latter and determined the concentration in it of amyl alcohol. This amounted to 0.0394 molar value, while in the original solution it was 0.0375. There was thus an increase of at least 5 per cent. in the concentration at the surface. This method of determination left out of account the fact that in such solution system the lowest surface tension was not at the air-solution surface but at the glass-water surface, and, consequently, the concentration at the air-solution interface would be less than it would be if the fluid system were wholly surrounded by air. Further, the films forming the foam do not consist wholly of the fluid of the successive adsorption layers, and, therefore, the ascertained surface concentration must be less than the actual.

The problem has more recently been dealt with in new and ingenious methods by M. C. M. Lewis (65, 66, 67), and the results obtained are of surpassing interest, not only on the chemical and physical sides but also and more particularly, on the physiological. On account of this special interest a detailed statement of the methods and the results is in place here.

The surface of condensation in which he estimated the concentration of the solutes was the interfacial surface between a hydrocarbon oil and an aqueous solution, or between mercury and such a solution. The hydrocarbon oil or the mercury was in the form of droplets or spherules, each in contact on all its superficial area with the aqueous solution, and on their surfaces the concentration of the adsorbed solute was experimentally ascertained and compared with the value determined from the equation

$$\Gamma = -\frac{C}{RT} \cdot \frac{d\sigma}{dC}$$

The hydrocarbon oil as well as the mercury was employed because they do not absorb or take up in themselves any trace of any one of the solutes in the solution bathing the surfaces of the droplets.

In the case of the hydrocarbon oil it was employed in two ways—as an emulsion with the aqueous solution, or it was allowed to ascend as droplets through a tall column of the solution. In the first case a certain quantity of the oil, mixed with a known quantity of the aqueous solution, was agitated in a shaker for some hours. The result was an emulsion in which the droplets or spherules were all of nearly uniform diameter which was measured under the microscope. From this the average volume of each, as well as its surface, was determined, and, knowing the total volume of oil present, the total number of droplets was ascertained. The united surfaces of all could, accordingly, be found. The quantity of the solute in the emulsion, apart from the interfacial surfaces, was ascertained by an adaptation of the drop-pipette or stalagmometric method.* The difference between the two concentrations thus known was attributed to adsorption on the united superficial areas of all the droplets, and thereby the concentration on each cm.^{2} of interfacial area was determined.

In the second method the hydrocarbon oil was allowed to ascend through a long column of solution in a tall cylinder, which terminated above by a minute tap in another short, but broad, cup-like vessel containing a quantity of the same solution. The oil drops could freely ascend through this tap and through the supernatant fluid to its surface, but a free backflow of this fluid into the cylinder was minimized. In this apparatus the volume of oil used was accurately known, the droplets formed from it passed slowly up through the column of fluid, and their number was estimated from an average of the counts made for a representative period. When the oil drops had all ascended, the communication with the cup-like vessel was cut off by compressing a rubber joint just below the latter, the fluid in the cylinder, the amount of which was accurately known, was run off from a tap below, and the concentration of the solute in it determined as in the other method. The difference between this concentration and the original one, the total volume of the solution in the cylinder and the united surface areas of all the oil droplets which passed up through the solution, gave all the factors which permitted a determination of the concentration of the solute on each cm.^{2} of the interfacial area.

When the mercury was used instead of the hydrocarbon oil it was allowed to fall in uniform droplets through a tall column of a solution in a cylinder which terminated in a reservoir below, from which it could, however, be shut off by turning a tap. The quantity of mercury used was accurately known, the number of its droplets which passed down through the solution was determined from an average of the counts made, and this gave the total superficial area of all the droplets. The original concentration of the solution being known, and having also determined the final concentration, the difference gave the amount of the solute abstracted from the quantity of the solution in the cylinder, which was also known. From all these data the amount of the solute adsorbed on each cm.^{2} of the interfacial area was determined.

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* For an account of which see the original memoirs.

The solutes used in these experiments were sodium glycocholate, methyl orange, Congo red, sodium oleate, caustic soda, silver nitrate, potassium chloride, barium chloride, copper chloride, caffein and anilin, and these were used in different concentrations. In only the last two named, caffein and anilin, did the directly ascertained values for surface condensation approximate those which the formula

$$\Gamma = -\frac{C}{RT} \cdot \frac{d\sigma}{dC}$$

postulated, while in all the others the values determined by the experimental methods used far exceeded the theoretical values. In the case of sodium glycocholate of 0.25 per cent. concentration used with the hydrocarbon oil, the surface concentration was 5×10^{-6} grm./cm.^{2}, but the theoretical value was only 7×10^{-8} grm./cm.^{2}, that is, the directly ascertained value was about 70 times the theoretical value. When mercury was used in place of the hydrocarbon oil the sodium glycocholate adsorbed at the mercury-solution interface was 25 times the value calculated from Gibbs' formula. In sodium oleate the directly determined value was 100 times the theoretical. In Congo red, methyl orange and caustic soda used with oil, the factors were 25, 43, and 20 respectively. If even considerable allowance is made in each case for errors of determination the excess was still so great as to lead Lewis to suggest, as a possible explanation, that the adsorbed material occurred in a gelatinized or colloidal condition on the oil or mercury surface. In the inorganic salts used there was also an excess adsorbed over the theoretical value, but it was chiefly the cation that was so affected. In silver nitrate the silver adsorbed was about 5 times in excess, in copper chloride the copper was 17, and in potassium chloride the potassium adsorbed exceeded by 30 times the calculated amount. This excess is, in Lewis' opinion, probably due to electrical effects, since the oil used is negatively charged, and the potential difference between the oil and water is approximately 0.05 volt.

The significance of these facts may appear a little more striking on further analysis. As pointed out above, the diameter of a water molecule is 3.39×10^{-8} cm., and, therefore, the diameter of its sphere of attraction at the oil solution interface would be 6.78×10^{-8}cm., but Lewis, accepting the range as equivalent to that postulated by Parks (86), namely, 13.4×10^{-6}cm., and using also the value, 5.4×10^{-6} grm., for the amount adsorbed per cm.^{2} from a 0.25 per cent. sodium glycocholate solution, as experimentally obtained, calculated that the concentration of the bile salt in the superficial layer was 40.3 per cent., or 160 times at least that obtaining in the rest of the solution. If, on the other hand, we assume the range of molecular attraction to be lower than that postulated by Parks, then the concentration of the bile salt at the interfacial surface must be extraordinarily high.

It is, however, not certain that the solute adsorbed is confined to a deposit within the range of attraction of the molecules on the interfacial surface. It is probable that there is no sharp break between the concentration at the interfacial surface and in the solution generally—that, in effect, there is a shading off between the two. It is true that the amount adsorbed depends on the surface tension of the interfacial area whose effects do not extend beyond the range of molecular attraction, but in the case of the solutes which are adsorbed in such extraordinary excess as to suggest the formation of a colloidal or gelatinous deposit, the latter must tend to produce successive, superposed, interfacial surfaces till equilibrium is attained, in which case the deposit may extend with lessening concentration through a distance from the original interfacial surface equivalent to several times the range of molecular attraction.

Such facts as these make it clear that surface tension is a very important factor in osmosis. In osmotic processes interfacial surfaces are conditioned, and, consequently, surface tension participates. When a membrane separates two fluids, one a solution and the other the pure solvent, there will be adsorption on the membrane-solution interface, whether the surface tension of the solution be higher or lower than that of the pure solvent, and, in consequence, there will, at the outset, be inequality in the distribution of energy between the two sides of the membrane. On the principle that energy everywhere tends to a minimum, there will be a movement from one side of the membrane to the other, and in the vast majority of cases at first from the pure solvent to the solution. That it will not always be in the one direction has been shown by Dutrochet (27), Graham (44) and Flusin (30), who found that in the case of certain solutions with animal membranes the movement, at the outset, was from the solution to the pure solvent. Graham found that solutions of oxalic, citric, tartaric and hydrochloric acids, of the chlorides of gold, tin and platinum and of nitrate of magnesium gave this result, and he accordingly called it negative osmosis. Flusin points out that an aqueous solution of tartaric acid in which the surface tension is lower than that of pure water, moves through an animal membrane to the pure solvent, that is, from low to high surface tension.

Such facts as these show that osmosis is not the simple process postulated by the gas theory of solutions formulated by van 't Hoff, and that surface tension enters as a factor in the result, though not to the full extent demanded by Traube (104, 105, 106, 107, 108). The latter holds that surface tension is all-important in osmosis, and that it operates through the attraction pressure (Haftdruck) of a substance which determines the velocity of the osmotic movement and the direction and amount of the osmotic pressure. The Haftdruck of a substance is measured by the effect that substance exercises on the surface tension of the solvent, or, to put it in Traube's own way, the more a substance lowers or raises the surface tension of a solvent the less or greater is the Haftdruck of that substance. Neither this view nor the currently accepted explanation of osmosis suffices, but the merit of Traube's crusade consists in the fact that it has directed attention to the part that surface tension plays in osmosis, a factor that has been, and is still, wholly ignored by those who hold rigidly to the gas theory of solutions.

It may be held that, after all, it is the pressure of the solute in a gaseous condition that determines its condensation on an interface where the surface tension is low, and that, therefore, the gas theory of solutions fully serves as an explanation of the osmotic processes. It is, however, surface tension that introduces this inequality of distribution of the solute, and this inequality may profoundly alter the conditions at the surface of a membrane. The force that causes this inequality must affect, also, the other side of the membrane, if the latter is permeable to either solvent or solute and both solvent and solution wet it. Further, if when the adsorption does not in amount exceed that determined by Gibbs' equation,

$$\Gamma = -\frac{C}{RT} \cdot \frac{d\sigma}{dC},$$

the surface concentration is a factor to be taken into reckoning, what must it be when it greatly exceeds that amount, as in the case of bile salt, seventy times? Such extraordinary concentrations cannot but have a marked effect in influencing the force and direction of osmotic currents.

Surface tension, then, must be one of the factors in osmosis. Under purely physical conditions it must play an important part, but, as I shall show later in this communication, that part is all-important in physiological osmosis.

Before concluding this section it is well to comprehend clearly a few special applications of the principle of surface tension. In the preceding pages the fluid system that was referred to had only one interface, as the drop of water suspended in space and unacted on by gravity. In such a system the solutes that lower surface tension would concentrate at the air-water surface, while those that raise surface tension would be found less concentrated at that surface than in the rest of the system. A fluid system under such conditions does not, however, occur in either the physical or physiological worlds. The systems which one ordinarily finds are those which have ununiform, interfacial conditions, that is, the surface tension is not uniform over their surface.

This has a special effect on the distribution of the solutes, as may be illustrated by the case of water in a glass vessel. Here there are two different interfaces, one of the water-air surface, the other of the water-glass boundary. The tension at the water-glass surface is less than that of the water-air surface. This is due to the fact that the molecules of the glass, coming as they do in closer range than do those of air with the superficial molecules of the water, diminish more markedly their free energy and, accordingly, the surface tension.

If, now, a solute is present it will be concentrated most at the interface having the lowest surface tension, i.e., on the solution-glass surface. This happens whether the solute lowers or raises the surface tension of the water. If it lowers the surface tension it will be concentrated least in the body of the solution, more at the solution-air surface and most at the solution-glass surface, for the surface tension of the pure solvent at the latter point, low as it is, is lowered still more by the solute. Further, in such a system the solute which raises the surface tension at the water-air surface should also raise that at the water-glass surface, but the two tensions would not be equalized, and, consequently, the solute would be least concentrated at the solution-air surface and most on the solution-glass interface. It would thus happen that if two solutes were present, one raising, the other lowering, the surface tension of the solvent, both would be most concentrated at the water-glass surface.

This explains the Thomson-Monckman experiment of filtration through surface tension. In this a solution of potassium permanganate is allowed to percolate through a layer of clean sand, and if the layer is of sufficient thickness the fluid that first issues is pure water, the solute having been retained by adsorption on the surfaces of the sand particles. A solution of bile salt similarly used would less readily issue as pure water, for there would, in such a percolating solution, be also a concentration at the water-air surface (owing to the fact that bile salt lowers the surface tension of water) though not as marked as at the solution sand surfaces.

It explains, also, the condensation of solutes on the surfaces of oil droplets or on droplets of mercury in a solution whether the solutes raise or lower surface tension, as in the researches of Lewis referred to. One is, further, thus put in a position to understand some of the conditions which affect surface tension in tissues, for in these the cells and fibres form, with lymph and other physiological fluids, interfaces which make for surface condensation. But, before all else, in each of the cells themselves, the individual units of the vital machine, there are different interfacial surface tensions which are the results of the adjustment of energy throughout each cell, and these bring about inequalities in the distribution of solutes throughout its contents.

III.—THE METHOD OF STUDYING SURFACE TENSION IN LIVING MATTER.

From the preceding section it may be gathered how surface tension affects not only the form of a fluid system, but also the distribution of solutes throughout it, and from such a fluid system one may pass to living matter and apply that principle in explanation of some of its functions. In applying it there are, however, difficulties involved. It is certain that surface tension moulds the form of a protoplasmic mass, but that certainty does not come from direct observation, and is derived only as a deduction from all the facts known regarding living matter and the physical properties of a drop of fluid. It is, indeed, improbable that differences in surface tension will ever be demonstrated directly.

Indirectly they can be demonstrated, but even here the difficulties are great. The indirect methods are two, namely, that which takes count of changes of form, and that which depends on the demonstration of surface condensation of solutes. Changes of form, or irregularities of surface, when they occur, can, however, only occasionally be thus used, for it is not always possible to attribute them to differences in surface tension. In multicellular organisms the cellular elements may be subjected to pressure, and there may thus be irregularities of outlines in which surface tension has not been a factor in the least degree. This method, therefore, except in unicellular organisms and in certain tissue elements, to be referred to later, is not one on which much emphasis may be laid.

The method which depends on the demonstration of surface condensation is of a wider application, but it is also of very great difficulty. In a drop of an aqueous solution on a glass plate surface condensation occurs, but it is difficult, nay impossible, to demonstrate it directly. In structures, like cells, in which viscidity and density produce, as compared with a pure fluid, stability of form, there are also difficulties. These arise, in large part, from the fact that we have no reactions which will show the presence of some of the substances adsorbed. In the chemical processes of cells a very large number of substances are produced which alter the surface tension of the cells, and, in consequence, they undergo adsorption at the surfaces where low tension is brought about. All these substances are beyond our present methods of microchemical demonstration, and, consequently, their adsorption cannot be shown. Along that line, therefore, little progress appears possible, at least for the present.

We are, however, not wholly resourceless in this difficulty. Amongst the inorganic salts that usually accompany, or are a part of, living matter, there are some whose elements can be demonstrated by definite and very delicate microchemical reactions. Of these, one is haloid chlorine, which, with a solution of nitrate of silver in dilute nitric acid and after exposure to sunlight, gives a reaction which will show the presence of 1 part of haloid chlorine in 3,000,000 of solution (Macallum, 74). The reaction is thus exceedingly delicate, and its only defect is that the reagent does not penetrate protoplasm rapidly enough in every case to be instantaneous. This makes the reaction ineffective, in some cases, as a means of demonstrating the surface condensation of chlorides in the protoplasm of cells.

This defect does not obtain in the case of the reaction for potassium. Some nine years ago (1903) the author discovered that the hexanitrite of cobalt and sodium, when employed in a certain concentration in a solution of sodium nitrite and acetic acid, constitutes a very delicate and instantaneously precipitating reagent for potassium, and that this reagent rapidly penetrates animal and vegetable cells (Macallum, 71). By freely washing the tissue or cells treated with the reagent in ice-cold water the reagent is removed, and the precipitate, consisting of the hexanitrite of cobalt, sodium and potassium, wherever it exists in a cell, appears as a cobalt yellow deposit. Of this precipitate only about 16 per cent. is potassium. On treatment with ammonium sulphide the cobalt is turned into the black sulphide of cobalt, which is a more striking indication of the presence of potassium than the original cobalt yellow colour. If now the preparation is mounted in glycerine it can be examined under the microscope. In this way the distribution of potassium throughout normal animal and vegetable cells has been ascertained by the author, whose experience with the reagent for the last seven years has convinced him that we have in this method a most valuable one for determining the distribution of potassium in connection with living matter.

The method, used on cells and tissues of representatives of all divisions of the animal and vegetable kindgoms, shows that potassium is very abundant in vegetable cells, as a rule, that it is present in the tissues of multicellular animal organisms, and that it is scanty only in the majority of Protozoa. In some organs in Mammals potassium exceeds the sodium in amount. This is the case with the brain, kidney, muscle and pancreas. In the tissues generally, whether animal or vegetable, potassium would appear to be abundant enough and to be widely enough distributed to serve as a means of determining the occurrence of adsorption and, therefore, of differences in surface tension.

The observations of eight years ago (Macallum, 71) demonstrated that potassium does obtain in local deposits and concentrations, the occurrence of which the author at the time did not explain. Potassium is not known to form precipitates in either the physical or physiological worlds, and yet aggregations and condensation found in animal and vegetable cells seemed to imitate precipitates. It occurred to the author that these condensations were the result of the action of the Gibbs-Thomson principle, but owing to the novelty of the idea involved, and also because of the desire to investigate the matter further, that explanation was not then advanced, and the aggregations and local concentrations observed were referred to as "physiological precipitates" and "physiological condensations".

A more careful consideration based on widely extended observations on the distribution of potassium in animal and vegetable cells, carried on during the last six years, has fully convinced the author that these condensations of its salts are the result of the action of surface tension, that they are in nearly every instance the result of the action of the Gibbs-Thomson principle, and hence, that in the distribution of potassium in tissues and cells, as revealed microchemically, we have a means of detecting differences in surface tension.

This conclusion the author advanced two years ago (72), and on the basis of the observations made along this line endeavoured to explain all the leading vital phenomena as arising in part at least from changes in surface tension of the structures concerned in the production of these phenomena. The latter included the contractile action of protoplasm and muscle fibre, smooth and striated, glandular secretion, intestinal absorption, the generation and transmission of nerve impulses and the processes of cell division. The subject is a vast one, but the discussion of it on that occasion was necessarily very brief, and, therefore, only a few of the facts which have been obtained on this point were referred to. It is now opportune to deal more fully, though not adequately, with all the problems involved, and in the following pages it will be shown how the Gibbs-Thomson principle of surface condensation may aid us in explaining the causation of some of the vital phenomena.

IV.—SURFACE TENSION IN LIVING STRUCTURES.

(a) IN CELLS IN GENERAL.

Though surface tension as a physical force has been known since 1751 when Segner introduced it as a concept in physics, it was only more than a century later when it was first conceived as a factor in cellular action. In 1869 Engelmann (29) briefly explained the amœboid movement of protoplasm as due to forces quite the same as those "welche jeden nicht kugligen freien Flüssigkeitstropfen kuglig zu machen streben".

In 1876 Bütschli (20), almost equally briefly, sought to establish the hypothesis that surface tension is a very active factor in cell division.

Rindfleisch (96) in 1880 advanced views on protoplasmic movement in which forces were referred to that involve surface tension. According to this observer, the reticular and interstitial fluid parts of the cytoplasm are in intimate and static relation (adhesion), and disturbance of this relation results in movement. That the adhesion which he postulated is the result of surface tension is shown by one of the illustrations he used in explaining the operation of the adhesive force. He pointed out that a thin film of oil on water will exhibit movement if the water is heated. These movements, in the opinion of Rindfleisch, are due to disturbance of the force of adhesion between the two fluids, but, as is well known, they are caused by diminution of their surface tensions.

Berthold (13) six years later (1886) explained the streaming of the cell sap in vegetable cells as due to surface tension. Local changes in the surface tension on the boundaries between the cell plasma and the sap brings about spreading movements of the sap over the surface layer of the plasma, and the streams resulting may be confluent, or the most vigorous one absorbs the others or alters their direction. In this way Berthold accounts for the rotation movement which such streaming usually exhibits. He held, however, that the streaming and movements in Amœbæ and Plasmodiæ are not to be explained as due to the same causes. This did not essentially involve a denial of the participation of surface tension in the streaming and movements of animal cells, for in his view the protoplasm of an Amœba, when in movement, conducts itself somewhat as a drop of fluid does when it spreads out on a solid surface, and we know the forces engaged in the latter case are those of surface tension. The distinction, therefore, between the streaming and movement of animal protoplasm, on the one hand, and the same phenomena in vegetable cells, on the other, in Berthold's hypothesis, is based, in the last analysis, on differences, not of principle, but of degree.

In 1888 Quincke (90) applied the principle of surface tension in explaining all protoplasmic movement. He assumed the presence of oil and soaps in all cellular structures, and on account of this presence the cell protoplasm has special properties which can be illustrated in the case of oil with water. When a drop of oil lies on the surface of water it is acted on by surface tensions of three interfaces. The surface tension of the water-air interface is the greatest, while the surface tension of the oil-water interface is least, and that of the oil-air interface intermediate in amount.

The strongest tension, that of the air-water interface, will therefore pull out on all sides the drop of oil, and it will, in consequence, spread out into a thin film over the surface of the water. Now in cells surface tension operates, as in the distribution of oil on water, in spreading the protoplasm containing, as pointed out, oils and soaps, over surfaces in which the tension is greater. As soap is constantly being formed in protoplasm the surface of the protoplasm containing it, having a low tension on the protoplasm-water interface, will as constantly keep moving, and as a result the protoplasm will be pulled out with it. The movement of the protoplasm thus produced will be continuous, and thus constitute protoplasmic streaming. Cellular masses, thus partially or wholly enclosed in lamellæ containing soap or oil and surrounded by water, would throw out pseudopodia or manifest amœboid movement. The formation of oil or soap films at a point on the surface of a cell is thus the primary factor in movement.

Bütschli (21) in 1892 published the results of his observations on the movements of a drop of concentrated soap emulsion, which he explained as due to the layer of soap at a point on the surface of the drop dissolving in the water and lowering the tension of the water at that point. The water molecules on the water-emulsion interface elsewhere on the drop exert their tension, and thus occurs a streaming away from that point over the surface of the drop. This produces a corresponding movement in the drop at its periphery, and a return central or axial stream directed to the point on the surface where the solution of the soap occurred, and where now a protrusion of the drop takes place resembling a pseudopodium. In this manner, Bütschli holds the contractile movements of Amœbæ are brought about. In these the chylema or fluid of the foam-like structure in the protoplasm is alkaline; it contains fatty acids, and, in consequence, soaps are present which, through rupture of the superficial vesicles of the foam-like structure at a point, are discharged on the free surface. This produces there the diminution of surface tension that calls forth currents, internal and external, like those which occur in the case of the drop of soap emulsion.

As regards Quincke's explanation of protoplasmic movement and streaming, Bütschli has shown that it is based on a mistaken view of the structure of the cell in Chara and other plant forms in which protoplasmic streaming occurs. Bütschli's own hypothesis, however, is defective in that it postulates a current in the fluid medium just outside the Amœba and backward over its surface, the existence of which Berthold denies and Bütschli himself has been unable to demonstrate even with the aid of fine carmine powder in the fluid. He did, indeed, observe a streaming movement in the water about a streaming Pelomyxa, but the current was in the direction opposite to that demanded by his hypothesis. Further, his failure to demonstrate the occurrence of the postulated backflow in the water about the contracting or moving mass of an Amœba or a Pelomyxa makes it difficult to accept the hypothesis he advanced to explain that backflow, namely, that rupture of peripheral vesicles (Waben) of the protoplasm occurs with a subsequent discharge of their contents (proteins, oils and soaps) into the surrounding fluid. Surface tension, moreover, on this hypothesis would be an uncertain and wasteful factor in the life of the cell. On a priori grounds, also, it would seem improbable that this force should be generated outside instead of inside the cell.

A somewhat clearer view of the action of surface tension in Amœbæ was advanced by Ryder (98) in 1894. This observer regarded every detail in the form of the cell and its nucleus as determined by surface tension, and even attributed the formation of the rays of the aster in mitosis to the same force. It is the surface tension of the protoplasmic mass itself which operates in determining the external form of the cell. Owing to metabolic (chemotropic) changes at a point on the surface, the surface tension lessens there, a "rupture" of the superficial film takes place, and a flow of the protoplasm through the opening occurs. The new superficial film of the protrusion or pseudopodium thus formed may itself be of such weak tension that, like its predecessor, it also "ruptures" and the protrusion is extended. The flow into the protrusion is from the more central parts of the mass, and to replace this there is a flow inward from the protoplasm at the opposite pole. The whole movement thus resembles that of a vortex ring with which Ryder compares it, but the resemblance is not complete, for in the cell the centre of the ring is occupied by the current of protoplasm flowing through the weakened or "ruptured" membrane. The cell is thus flowing through itself, and the outer layers of molecules thus form a sort of shell or tunnel through which the central current flows. The special point in Ryder's hypothesis is that it postulates that it is the surface tension of the protoplasm itself and not of the surrounding medium that is the primary factor in producing movement.

A similar view was propounded by Verworn (109). He explained the diminution of surface tension which precedes the formation of pseudopodia as due to the oxidation of certain constituents (biogen molecules) of the protoplasm at the point.

Rhumbler (93, 94, 95), who adopted and expanded the views which Roux had advanced to the same effect, explained protoplasic movement as due to surface tension affected by inequalities (Anhomogenitäten) of composition and density of the surface layer as well as of the deeper portions of the protoplasmic mass. These inequalities are constantly changing, disappearing at one point to reappear elsewhere, and this tendency to change is favoured by the vesicular (schaumige) character of living matter which Rhumbler, following Bütschli, accepts as the normal structure of protoplasm. Each vesicle (Schaumraum) is a chemical laboratory by itself, and as the wall of each is composed of colloid material through which the diffusion of other colloid substance is difficult or impossible, all the vesicles will then be so many minute and independent laboratories, each with a product slightly different in amount and quality. In consequence of the action of the products of each vesicle the surface tension is affected unequally over the surface, which Rhumbler represents as a mosaic constituted of different fluid colloids, each of which has its own capillary constant. The changing products of the vesicles, as well as the changing activities of the latter, continually and unequally affect the surface tension, with the result that the great differences in form and contour of living matter which we comprehend under contraction and extension develop.

Not greatly different from Rhumbler's view is P. Jensen's explanation (55) of the causation of protoplasmic movement. According to the latter, vital movement of all kinds, muscular as well as amœbic, is due to alterations in surface tension brought about by metabolic processes in the cytoplasm. When the assimilatory (anabolic) processes predominate at a point in the cell, there results an increase there of the number of metabolities and a consequent decrease of surface tension. This leads to expansion at the point, and there pseudopodia form. When, on the other hand, the dissimilatory (catabolic) processes are specially enhanced, there is a decrease in the number of molecules, the surface tension at the point increases, and accordingly contraction develops. It is of course impossible to demonstrate the occurrence of these metabolic processes simultaneously with changes of form in unicellular organisms, and, in consequence, Jensen relies for support of his view on the fact that in muscle catabolic processes are coincident with contraction while the anabolic processes are enhanced during relaxation.

Brailsford Robertson (97) explained protoplasmic movement as caused by augmentation or diminution of contact difference of potential between the surface of the amœboid organism or the surfaces of cilia and the fluid medium by which they are bathed. This contact difference of potential is due to the presence of ion-proteins in the surface layer of the organism, and alterations in potential lead, as in mercury drops surrounded by sulphuric acid, to local alterations in surface tension and, consequently, to movements in definite directions.

Some observations bearing on the relation of surface tension to toxic action on living cells and to osmosis may now be detailed

J. Traube (104) pointed out, in the case of the primary monatomic alcohols of the fatty series and of the esters of these alcohols with acids of the acetic series, that the toxic effect of these substances increased in homologous series with their surface tension effect in the proportion of 3; e.g., each member of the alcohol series is three times as effective in its capillary action and three times as toxic as the next lower member of the same series. A quite similar relation was determined by Fühner and Neubauer (38, 39) in the action of alcohols in promoting hæmolysis, and J. Loeb (68) found it to obtain in the action of alcohols on the heliotropism of Copepods.

Czapek (22) has investigated the action of solutions of a number of substances in promoting the diffusion of tannin from vegetable cells, and has found that it depends on surface tension. The presence of tannin was demonstrated microchemically by treatment with a solution of caffein which forms myelin-like droplets with tannin. Solutions of acids of concentration exceeding $\frac{N}{6400}$ and of alcohols, ethers, chloroform, esters, acetone, ketones and urethanes in certain concentrations in water, when applied to the cells of Echeveria, Saxifraga and Spirogyra, cause the tannin to diffuse from the cells, and Czapek determined that the concentrations of the latter class of compounds gave the solution, in each case, a surface tension of 0.68-0.69 times that of water at 15-19°C. With methyl alcohol the concentration which gave this tension was 15 per cent. (i.e., 15 volumes of methyl alcohol per 100 of solution), with ethyl alcohol it was 10-11 per cent., with normal propyl and isopropyl alcohols between 4 and 5 per cent., with normal butyl and isobutyl alcohols between 1 and 2 per cent., and with amyl alcohol 0.5 per cent. The diffusion of tannins from the cells was, therefore, independent of the chemical composition of the substances.

With solutions of a higher surface tension exosmosis, or diffusion from the cells, did not occur. Czapek, therefore, suggests that the plasma membrane around the cells has a surface tension of 0.68-0.69 times that of water, and that so long as the exterior surface of the membrane is ordinarily bathed by a fluid whose surface tension is greater than the above value, which he calls the critical tension, no diffusion occurs. Osmosis then depends in this instance on the establishment of a critical surface tension in the external fluid. The determination in any particular case of the critical tension would, Czapek holds, thus reveal the surface tension value of the plasma membrane.

From the foregoing account of the literature on the subject it may be seen to what extent in the past surface tension has been regarded as a factor in cell life in general, and how largely the views advanced are derived from speculation and theory alone. It was inevitable that they should be largely so derived, for, as already indicated, there was, apart, it may be, from the alterations in form of living matter, no direct evidence of the participation of surface tension in vital movement.

The observations which are now to be advanced as bearing on this question arise from the application of the Gibbs-Thomson principle of surface condensation in explanation of the distribution of potassium in animal and vegetable cells as determined by microchemical methods by the author.

The most striking instances of the surface condensation of potassium are to be found in the Protophyta and especially in Spirogyra, Mesocarpus, Mougeottia and Ulothrix.

In Spirogyra the potassium is condensed in the immediate vicinity of the chromatophor. When the turns of the latter are very closely applied, then the spaces between the adjacent turns appear charged with potassium. When, however, the turns of the spiral are far apart, as in Fig. 1, the potassium is found confined to either margin of the chromatophor. There is so little potassium in the rest of the cell that no reaction for it was obtained with the hexanitrite reagent. The condensation on the margins of the chromatophor must accordingly imply that in this part of the cell, that is, on the chromatophor-cell sap interface, the surface tension is low as compared with other interfaces inside the cell membrane. As the synthesis of carbohydrates takes place in the chromatophor under the influence of sunlight, and as potassium is a factor in bringing about that synthesis (*vide infra*), it would appear that low surface tension is a factor in that synthesis, or is a result of the synthetic processes producing substances which, in themselves, lower surface tension. If formaldehyde is a product in the course of this synthesis it must lower surface tension. It may possibly be that the low surface tension is both a factor in the synthesis and a result of the processes involved.

When conjugation occurs in Spirogyra the outgrowth from either cell to form a zygospore is preceded by an accumulation or condensation of potassium at the point immediately under the cell wall where the future outgrowth is to develop. The cell wall soon develops a convexity at the point, to which the cytoplasm accommodates itself, and at the same time the potassium condensation becomes more marked. While the growth continues the potassium condensation obtains in its tip, but when the outgrowth meets the corresponding growth from the neighbouring cell and the contiguous membranes disappear, permitting the cytoplasms of the two outgrowths to fuse, the potassium condensation quickly resolves, and the element, or rather its salts, diffuses throughout the mass of the protoplasm derived from both cells that is to form the zygospore. The latter thus gets its potassium from the condensation at the tip of each outgrowth. The whole history of the process of conjugation thus demonstrates a surface condensation of potassium due to a surface tension lower at the outgrowth than obtains elsewhere in the cells.

When the quantity of potassium present in the conjugating cells of Spirogyra is small then the surface condensation of potassium in the tips of the outgrowths is very scanty and may even be absent. This, however, does not happen in normal Spirogyra.

In Mesocarpus during conjugation a similar condensation of potassium obtains. The mode in which the outgrowths to form the zygospore develop is somewhat different from that observed in Spirogyra. The cells taking part become more convex on one face, and the convexity may embrace the whole length of the cell on that side (Fig. 3). Just inside the membrane at the central or most prominent part of the convex surface the potassium is concentrated densely in a mass which, from the intensely black reaction for cobalt sulphide which it gives, stands out very prominently as a cap-like structure. A later stage of the conjugation as well as of the condensation is represented in Fig. 4.

In the tips of the growing points in Cladophora, Vaucheria, Œdogonium and Nitella, potassium, when present, is frequently found condensed in a thin layer immediately under the membrane at the very extremity of the growing cell, while the remainder of the cell is free from it.

In Ulothrix one very commonly obtains specimens in which the potassium is condensed at the ends of the cells (Fig. 5), but the most marked occurrence of such condensation is to be found in a form that usually accompanies Zygnema, especially in the later months of summer. The author has been unable to diagnose the genus to which this form belongs, and, therefore, it must suffice to indicate its characters by reference to Fig. 6. In this form one sees, immediately adjacent to and on each side of the transverse wall of the confervoid thread, a most striking condensation of potassium. Here, as in the previous instances described, the condensation layer is not always sharply limited on its two faces. In the illustration there are not a few prolongations of the condensation extending towards the protoplasmic mass to which it belongs, and which has, through the action of the reagent used (the hexanitrite of cobalt and sodium), shrunken somewhat from its normal limits. In such preparations as these the condensation of potassium described indicates that the surface tension is low at the ends of the cell, a conclusion that could be drawn perhaps from the shape of the cell, for if the surface tension were uniform over all the surface of the cell the latter would be spherical.

Throughout the cytoplasm in this form one finds the potassium gathered in condensation layers about spherical or other masses and the occurrence of such suggests at once that low surface tension is effective here also.

In the germinating spores of specimens of Equisetum arvense, grown in soil rich in potassium salts, the potassium is usually found remarkably localized. While the spore is unicellular the potassium is more or less uniformly distributed throughout the cytoplasm. In the first division the greater part of the potassium is gathered in one of the two daughter cells, and chiefly there at the pole opposite the other cell (Fig. 7, *a*) where the convexity of the surface is a little more pronounced than it is on any other point of the surface. At this point the primary root hair of the spore takes its rise, and as it grows out from the cell the potassium present accompanies the growth, and its distribution is in the superficial layer of the cytoplasm of the outgrowth and immediately beneath the covering membrane (Fig. 7, *b*). This distribution of the potassium leaves no room for any other explanation than that it is a condensation at the surface where the surface tension is lower than elsewhere.

In the other cell of the germinating spore which contains chlorophyll at this early stage the scanty amount of potassium present is condensed immediately under the membrane.

In spores derived from Equisetum grown in sandy soils or in other soils largely free from potassium salts, no trace of potassium condensation may be found at any stage of germination, and potassium may be wholly absent. These spores seem to possess all the capacity for development that the spores which are rich in potassium manifest. This would seem to indicate that potassium salts are inert in the metabolic processes of the cell which develops the primary root hair. It is, however, possible that the potassium endowment may, in the later stages of development, make an important difference in the viability of the organism.

The fact that when the spore divides and is constituted of two cells, nearly all the potassium originally present in the spore is now found in the cell which is to develop the primary root hair, is significant of differences between the two cells immediately before they divide. The condensation in one of the two separating halves is evidence that one half has a lower surface tension than the other.

In the cells of the higher plant forms and specially in the parenchymatous tissue one observes occasionally a distribution of potassium on a portion of the cell surface, which suggests very strongly that here also is condensation due to surface tension. An example of this is illustrated in Fig. 8, representing a mesophyllous cell from the Easter Lily (Lilium). These mesophyllous cells are subjected to pressure, and thus their shape is not wholly determined by surface tension. In the example illustrated the potassium is shown in a condensation layer at *a*, which would indicate that at that point the surface tension is least. At other points in the cell potassium is concentrated about or on the surface of spherical bodies in such a manner as to suggest surface condensation. One finds this concentration very common in the mesophyllous and parenchymatous cells of leaves and stems, and later in the summer in annual plants the concentration of potassium thus brought about is remarkable. It is, indeed, in this way that the cells of the leaves dispose of the ever-increasing quantity of potassium brought to them by the transpiration currents from the roots throughout the whole season. If it were not for the condensation of the potassium salts on the surfaces of masses in the cytoplasm where the tension is low, the whole cell would be uniformly charged with potassium, and thus, perhaps, a toxic condition would be induced. On this view surface condensation due to surface tension enables the chlorophyll-holding and other cells of leaves to dispose of very large quantities of salts of potassium and other bases, for the surface condensation cannot be supposed to be confined to the potassium compounds, although the condensation of other salts is not demonstrable microchemically.

In the stomata of Tulipa one finds surface condensation of potassium as illustrated in Fig. 10. It is to be noted that the concentration is only on the convex surface of the "guard cells", the concave surface of each, i.e., that bounding the aperture between the cells, being wholly free from potassium. As these "guard cells" are supposed to alter their shape and thus open or close the aperture between them, one can comprehend in a measure how the alteration is effected. The most convex surfaces are endowed with the lowest surface tension, and this explains the concentration illustrated. When the aperture closes the concentration of potassium at the outer side of each cell becomes much less or disappears wholly, and the potassium is more uniformly distributed throughout the cytoplasm.

Weevers (114) has described and figured a localization of potassium in the tips of the root hairs of Hydrocharis Morsus ranæ, which is apparently a condensation due to the low surface tension at these points in the hairs, but that author, not having taken account of surface tension as a factor in such a situation, explains the localization as due to the potassium salts diffusing from the cytoplasm of the hair cell to that in the tip where it first meets the reagent which demonstrates its presence. What Weevers observed in this case may be paralleled in the tips of the growing points of the threads of Cladophora, Œdogonia, Nitella and other confervoid forms, and the conditions under which this localization is obtained excludes the explanation that it is due to such a factor as Weevers suggests.

As already stated, unicellular animal organisms are largely free from potassium. In Vorticella there is no potassium present except in the contractile stalk, in a minute deposit around the base of each cilium, and in very minute quantities in the cytoplasm immediately about the digestion cavity. There is indeed much more potassium in the stalk than in the main cytoplasmic mass or head, and it is there distributed throughout its length. This would indicate that the head is under higher surface tension than the stalk and the part of the head from which it extends. The occurrence of minute amounts of potassium immediately about the digestive cavity of the organism is an indication that the surface tension is low there also, though not perhaps to the same extent as in the stalk.

In Paramœcium the potassium present is minute in quantity. It is found in the ectosarc and confined to the basal portion of each cilium. On the Gibbs-Thomson principle low surface tension, therefore, is a factor in the production of these structures, a conclusion that is, on a-priori grounds, probable.

In spermatic cells in Vertebrates the distribution of potassium varies with the stage of development. In the spermatogonia it is condensed on, and in masses in, the cytoplasm in a manner that suggests surface condensation as a factor. This almost becomes a certainty in the case of spermatids. In Fig. 11, representing a spermatid from the guinea-pig, the potassium is shown massed under one portion of the surface of the cell. In the fully formed spermatozoid the potassium is usually wholly condensed in that portion of the original cytoplasm which envelops the posterior part of the head. In the ripe spermatozoa of the frog there is seen a similar distribution of the potassium. In the spermatozoa of the dog, as they exist in the tubules of the epididymis, there is very little potassium.

The occurrence of potassium at the base of each cilium in Paramœcium and Vorticella, in the stalk of the latter form, and its presence in the more or less unaltered cytoplasm about the posterior part of the heads of spermatozoa, are all related facts, and the connecting principle is surface tension which is, one must suppose, responsible for the development of the cilium and the stalk and for the shape of the spermatozoon. On this basis the motor or contractile function of all three may be referred to slight alterations of surface tension arising in the head of Vorticella or of the spermatozoon or in the ectosarc of Paramœcium and passing over the stalk, tail or cilium in a wave-like manner to its termination, the wave of low tension being only momentary in duration and being quickly succeeded by another of like character.

(*b*) IN MUSCLE FIBRE.

The first to discuss from the physical point of view the source of the energy of muscle contraction was G. F. FitzGerald, the Dublin physicist (33), who in 1878 advanced the view that it is due to surface tension. Assuming that in mammalian muscle each fibre is 0.05 mm. ($=50\mu$) in diameter and each fibre to consist of closely packed fibrils, each of which, to facilitate computation, was to be triangular in section, and further, that the side of each triangle was 0.000125 cm. ($=1.25\mu$), he estimated that there would be about 500 metres of circumference of fibrils per square centimetre of cross section of muscle. This, with a surface tension equal to that of water, would give a disposable force of 4 kilograms as against the then currently estimated value of 7 kilograms. By assuming also that the fibrils have each a smaller diameter, a much larger disposable force can be estimated, and, in consequence, diminished surface tension (i.e., much less than that of water) would be compensated by increased fineness of structure. He suggested that fibrils and transverse striæ are for the very function of developing surface tension, and also that the electrical disturbance accompanying muscular contraction affects this surface tension as differences of electrical potential in Lipmann's experiments with mercury drops affect the surface tension of the latter.

The next to suggest surface tension as a factor in muscle contraction was D'Arsonval (2), who was unaware of FitzGerald's observations and views. D'Arsonval, basing his idea of surface tension in muscle on the electro-capillary phenomena, constructed according to his views a physical model of striated fibre in the following fashion. In a rubber tube he placed mercury, dilute acid and discs made of pipe clay or porous porcelain, and these were so disposed that a disc, some mercury and then some dilute acid, all in this order, were repeated in series many times throughout the length of the interior of the tube. This model, hung vertically and attached above and below to wires from a battery cell, should, on the passage of a current through it, give a mechanical deformation or shortening of the model, due to the change of electric potential on the surfaces of the mercury drops altering their form or contour. An experiment demonstrating this result he did not describe, but he did show, by methods which need not be described here, that mechanical extension of the model gave origin to a current which could be felt.

Imbert (52) in 1897, referring to D'Arsonval's views as to the connection between surface tension and contraction, directly applied the principle in explanation of the contractility of smooth and striated muscle fibre. According to him the primary conditions are different in the two kinds of fibre. In smooth muscle fibre extension is determined, not by any force inside it, but by an external force such as may distend an organ (intestine, bladder or artery) in whose wall it is found. The "stimulus" which causes the contraction increases the surface tension of the fibre-lymph interface, and this of itself tends to make the fibre thicker and shorter, a change that occurs in contraction. He did not, however, explain how the stimulus altered the surface tension, except so far as to say that its effect on surface tension is like that of electricity, to which the nerve impulse presents some analogy. In striated fibre the singly and doubly refractive discs are in contact like two fluids, and their interfacial tension opposes the surface tensions of the external surfaces of these same discs. How these forces should operate is not quite clear from Imbert's description, but one gathers that the longitudinal diameters of the two discs at rest are due to the resultant effect of the different surface tensions. When a stimulus (nerve impulse) reaches the fibre the surface tensions of the discs are unequally altered and there results a deformation of each, involving primarily a shortening of its longitudinal axis and thus a shortening of the whole fibre.

According to Bernstein (9) there is, in both smooth and striated muscle fibre, in addition to surface tension, an elastic force residing in the material composing the fibre, which, owing to the conditions that may obtain, sometimes opposes and sometimes assists the surface tension. The result is that in the muscle fibre at rest the surface must exceed somewhat that of the fibre in contraction. In both conditions the algebraic sum of the two forces must be zero. In contraction the surface tension increases, and with it the elasticity also. Taken as a whole, this would not explain the large force generated in contraction, for the energy liberated would be the product of the surface tension and the amount of the diminution of the surface due to the contraction. As the latter is very small the product is much below the amount of energy in the form of work done actually manifested. To get over this difficulty Bernstein postulates that in muscle fibres, whether smooth or striated, there are fibrils surrounded by sarcoplasm, and that each fibril is formed of a number of cylinders or biaxial ellipsoids singly disposed in the course of the fibril, but separated from each other by elastic material and surrounded by sarcoplasm. Between the ellipsoids and the sarcoplasm there are considerable differences of surface tension which prevents mixture of the substances constituting both.

In order to account for all the energy of contraction these fibrils must be sufficiently numerous. To ascertain how many there may be Bernstein took the semi-membranosus of a frog, determined experimentally its absolute force, then hardened it in the extended condition in alcohol for a fortnight, after which it was imbedded in celloidin and transversely sectioned in the microtome. In such sections, making all allowances for the shrinkage due to alcohol, he found the average radius of each fibril to be 9.994×10^{-6} cm. and calculated that in a square centimetre of such a section there would be 31,460,000 fibrils which, with the data for elasticity and absolute force (3000 grms.), gave 0.022 grm. as the value of the surface tension of the fibril at its fibril-sarcoplasm interface. This value is very near that of oil at an oil-water interface, which is approximately what Bernstein supposed the surface tension of the fibrils to be. To provide, however, for a greater value of the absolute force he postulated a greater tenuity of the fibrils, of, e.g., a radius of 10^{-6} cm.

The excitation of the fibrils through a nervous impulse causes an increase of the surface tension of ellipsoids which, therefore, become more spherical. In consequence, the decrease in surface of all the ellipsoids constituting a fibril is much greater than if the fibril were to be affected as an individual unit only by an increase of surface tension, and thus the surface energy developed would be correspondingly greater. The ellipsoids, Bernstein explains, are not to be confused with the discs, singly and doubly refractive, in striated muscle fibre, for these, he holds, are not concerned in the generation of contraction, but with the processes that make for rapidity of contraction. The extension of a muscle after contraction is due to the elastic reaction of the substance between the ellipsoids in the fibril.

Bernstein holds that fibrils of this character, with ellipsoids and sarcoplasm, occur in the cytoplasm of Amœba, in the stalk of Vorticella and in the ectoplasm of Stentor, and this explains the contractility they manifest.

In accepting Fick's view that the muscle is not a thermodynamic but a chemodynamic machine, Bernstein points out that wherever in nature a transformation of chemical energy into mechanical energy takes place, this is brought about through the intermediation of volume energy, surface energy or electrical energy. Now, volume energy is excluded in muscle, since there is no change in volume of muscle when it contracts, while the electrical properties of muscle afford no support to the view that electrical energy contributes a part of the energy of contraction, and therefore, the only source of the contraction energy that is possible is surface energy.

It may be said in criticism of Bernstein's fibrils, that while they consist of ellipsoids, each fibril, according to his calculations, is supposed to act as if its surface were an individual unit, not a composite one which it must be if ellipsoids constitute the fibril. It is this feature that makes it necessary for him to postulate extreme tenuity of such fibrils and an extraordinarily large number of them in order to account for the amount of absolute force that a muscle (7000-10000 grms. per cm.^{2}) sometimes exerts. If each fibril were constituted of one hundred ellipsoids placed end to end, and if the surface tension of each ellipsoid were capable of change independently, then the surface energy of the whole fibril would be one hundred times that of the same fibril homogeneous and undifferentiated. Moreover, the ellipsoids from their very nature are non-demonstrable structures, and must always remain as postulated elements only. It may further be pointed out that Bernstein attributes too small a part to surface tension in the lengthening of the fibre after contraction, and that the elasticity which muscle appears to possess may, in the ultimate analysis, be but a result of surface tension.

Jensen (55), like Bernstein, explained the contractile phenomena of muscle as due to surface tension, this force with elasticity determining the form of the fibrils. Unlike Bernstein, he recognized the sarcous elements as primarily concerned with the generation of contraction. Surface tension operates between the isotropous substance and the sarcoplasm, between the anisotropous substance and the sarcoplasm, as well as between the isotropous and anisotropous elements. In relaxation of the fibrils the surface tension of these interfaces balances the elastic forces, but in contraction the surface tension constant of the fibrils is increased as a result of the chemical changes of the sarcoplasm and fibrillar substance affected through the stimulation. This leads to a mingling of the isotropous and anisotropous substances, the surface tension of their interfaces vanishes, and, in consequence, there results a diminution of the force that opposes shortening. The two substances thus form in each sarcous disc a common cylinder with proportionately larger surface which, however, is capable now of considerable diminution. The shortening and thickening of the fibrils, accordingly, develops till the different forces are again in equilibrium. In relaxation these processes happen in the reverse order.

As in the case of ordinary protoplasmic organisms so in muscle, Jensen holds, assimilatory (anabolic) processes decrease surface tension and dissimilatory (catabolic) processes increase it. The chemical changes involved in these dissimilatory processes are developed as the effect of the stimulus of the nerve impulse.

Brailsford Robertson (97) attributes the contraction of striated muscle to the elastic recoil of tubules composing the contractile fibrils, these tubules being, in resting muscle, pulled inwards and lengthened by the surface tension of their fluid contents. Ion-proteins exist in the walls of these tubules which, under the influence of stimulation, develop free inorganic ions. The latter augment the potential difference between the surfaces of the tubules and their fluid contents; in consequence, the surface tension of the fluid contents diminishes, and the walls of the tubules, partially released from the inward pull of the fluid contents, recoil and become shorter and more spherical.

From this review of the various theories as to the part that surface tension plays in muscular contraction, it may be seen that the basis of all is largely speculative, and that, highly ingenious as the theories are, there is but a small amount of ground common to all of them. There is no agreement on the point whether surface tension is diminished or increased in contraction. FitzGerald's observations suggest a decrease, the views of Bernstein postulate an increase, Jensen's theory predicates the abolition of it, while Brailsford Robertson's entails positively a reduction, though it is not implied that there is a diminution of surface.

Two years ago the author (72), in giving an account of views advanced regarding the derivation of muscular energy from surface tension, pointed out that we have, in some of the results of microchemical study of muscle fibre, evidence that surface tension is a factor in muscle contraction, and he discussed briefly the significance of this conclusion.

The evidence is derived from the distribution of potassium and haloid chlorine in muscle fibre. Both elements are present, but potassium is especially abundant. From the analyses of Katz it has been found that potassium is three and a half times in the striated muscle of the dog, and fourteen times in the muscle of the pike, as abundant as sodium. How the potassium salt was distributed in the fibre was unknown before 1904, in which year the author (71), by the use of the hexanitrite of cobalt and sodium as a microchemical reagent for potassium, found it localized in the doubly refracting discs of the fibres. Later and more extended observations suggested that in the doubly refractive disc itself the potassium is not uniformly distributed, and this was found to be the case in the wing muscles of certain scavenger beetles in which the discs are broad, and, therefore, conspicuous enough to permit of distinct observation on this score. In these fibres the potassium salt was found localized in the zone of each disc (sarcous element) adjacent to the light band. Subsequently, Miss M. L. Menten (83), using the same microchemical method, found the potassium limited in its distribution in the muscle fibres in a number of other insects. This distribution is in a band usually very narrow, in the sarcous element and ordinarily immediately adjacent to each light band. She determined also that the chlorides and phosphates have a like distribution in these structures, and it is, consequently, probable that sodium, calcium and magnesium have the same localization.

Macdonald (75) also, using the hexanitrite reagent for the microchemical demonstration of potassium, made investigations of the distribution of this element in the frog, crab and lobster, and as a result of his observations holds that the element in the uncontracted fibril is limited to the sarcoplasm in the immediate neighbourhood of the singly refractive substance, while it is abundantly present in the central portion of each sarcomere of the contracted fibril, that is, in the doubly refractive material.

As a criticism of Macdonald's results it may be pointed out that too great reliance is placed on preparations from the muscle of the frog into which the hexanitrite reagent only slowly penetrates, and, apparently because of this, alterations in the distribution of the salts occur, in consequence of which, as the author has repeatedly observed, potassium may be limited to the doubly refractive bands in one part of the contracted fibre and to the singly refractive discs in another part of the same. This is true in very large measure, also, for the fibres of the crab and lobster. Even in the wing muscle fibres of insects the same irregularity was observed by Miss Menten, but such disconcerting results are not so readily obtained in such fibres, owing, it would seem, to the readiness with which the fibrils may be isolated and the almost immediate penetration of them by the reagent. In such preparations from resting muscle fibre the potassium undoubtedly, in the vast majority of cases, occurs in a zone at each end of the doubly refractive band and immediately adjacent to the singly refractive band.

Whether the potassium is in the sarcoplasm or in the sarcostyle it is difficult to decide. It is not easy to apply in microchemical studies of muscle fibre the concepts of its more minute structure derived from the investigation of merely histologically stained preparations. All that can be accepted with any degree of certainty is that the potassium is limited to the sarcous elements which undoubtedly include some sarcoplasm.

A difficulty appears here which may be explained. The application of the hexanitrite reagent should, it may be held, convert the fresh muscle fibre from the resting to the contracted condition. This undoubtedly happens under certain conditions and especially when the reagent does not get immediate access to every fibril of a fibre. When the sarcolemma effectively interposes as a barrier, the irritant action of the reagent long precedes its fixative and precipitant actions, and, in consequence, the fibrils of the intact fibre may show only the contracted condition. To prevent this it is not of any service to keep the fibres stretched while the reagent is applied to them. Such fibres are extended fibres, not relaxed or resting, and they are exactly in the same condition as those of a muscle which is loaded so heavily that it can give no contraction at all, or only the slightest possible one. In this case the fibres have undergone the physical and physiological changes of contraction, but only the resultant effect of these changes, the shortening, has not been allowed to appear. One must, therefore, not regard the fibre extended while undergoing fixation as illustrating the fibre as it is in the physiologically relaxed condition.*

This makes it necessary to exercise very great discrimination in accepting, as illustrating the "relaxed" or "resting" condition, fibres which have been treated under any condition with the hexanitrite reagent. This has been borne in mind by the author in observations on the distribution of potassium in resting and contracted muscle fibrils.

Now, on applying the Gibbs-Thomson principle of surface condensation as a test for differences of surface tension, the distribution of potassium as described for the resting muscle fibrils of insects would seem to indicate that in the doubly refractive substance the greatest surface tension is in the lateral walls of the sarcous element, in consequence of which the potassium salts are concentrated on the other surfaces of the sarcous element, i.e., on the borders of the singly refractive discs. This conclusion would seem to be confirmed by observations which the author (71) made on the contracted fibrils of the wing muscles of a scavenger beetle. In these the potassium was found uniformly distributed throughout each doubly refractive band, which, instead of being approximately cylindrical in shape as in the resting fibril, was provided with a convexly curved lateral wall, and, therefore, with a smaller surface than the mass of the sarcous element has when at rest. This contour suggests that either the surface tension on the two end surfaces of each sarcous element is increased, or that the surface tension on its lateral wall is decreased to an amount below that of either terminal surface, and this is followed by a redistribution of the potassium salt to restore the equilibrium thus disturbed. The consequent shortening of all the doubly refractive discs in the fibril would account for the contraction of the muscle.

The production of a curvature on the lateral wall of the sarcous element during contraction is attested by many histological observations, particularly on insect muscle fibrils which can in the fresh condition be readily separated from each other, and in which, owing to the thickness of the fibrils and the lengths of their sarcous discs, the outline of the sarcous element in rest and during contraction can be observed. It may indeed be held, without undue emphasis being placed on the known facts, that the thickening of muscle during contraction is due to the assumption by the lateral walls of the sarcous elements of each fibril of a more convex curvature.

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*A very striking illustration of the contrast between uncontracted and stretched (extended) muscle fibrils from the wasp is shown in Schäfer's article (99), Fig. 1, B and C.

There does not, therefore, appear any reason to doubt that the sarcous elements change in shape during contraction, and, from the distribution of potassium in these structures during rest and as well as in contraction, it is certain that differences of surface tension are a factor in the change of shape, but it is not clear whether the change is due to an increase of surface tension on the terminal faces or a decrease of surface tension on the lateral walls of each sarcous element. The difficulty of deciding this is intelligible. If a drop of fluid suspended in space and unacted on by gravity were of itself to assume the form of an ellipsoid, it would be rightly inferred that the surface having the least curvature, that is, the side, would on the whole be under greater surface tension than the surface at the two ends of the ellipsoids possess. If, further, such a drop were for a moment to assume a more spherical shape, then one of two things happened: either the surface tension on the least curved surface decreased or the surface tension on the most convexly curved surface increased, but which of the two really occurred could only be determined when certain conditions were known. In the sarcous elements the conditions are all unknown, and we cannot, consequently, be certain whether the factor is an increase or a decrease of surface tension, although certain inferences may be drawn. Bernstein believes that the factor is an increase of surface tension in his ellipsoids. This could be brought about in only one of two ways. Either there must be an escape from the surface layer of the ellipsoids of a substance or substances which lower its surface tension, or there is an electrical double layer on the surface of each ellipsoid which lessens the surface tension, and when this electrostatic charge is diminished or abolished the surface tension is increased.

There is at present no evidence that substances escape from the surface films of the sarcous elements, nor could such an escape be accounted for if it did occur. On the other hand, we do not know that an electrical double layer exists at the surface of each sarcous element, although it is not improbable that such may normally exist; but if so, it must be excessively weak, for the lateral wall of a sarcous element in a fibril is under greater surface tension than its terminal walls, the surface tension of which, from the character of the interfaces at these points, must be low. To make this explanation effective, one would rather have to postulate a double electrical layer on the terminal interfaces of the sarcous elements which would be dissipated before the muscle fibril begins to contract.

The simplest explanation of the shortening of the sarcous element, after all, is that the surface tension on its lateral walls decreases. How that surface tension is lowered is a question which can be answered only when much more is known of the nature of the nerve impulse as it reaches the muscle fibril, and of the part played by the energy set free in the combustion process in the doubly refractive discs. It may be that electrical polarization, the formation of an electrical double layer, as a result of the arrival of the nerve impulse, develops on the surface of the lateral wall, and as a consequence of which its surface tension would be diminished. The diminution must be small, the decrease in surface area must be more than correspondingly small, and, therefore, the product of these two values, the surface energy, developed in contraction of a sarcous element of a fibril, must be very minute indeed. When, however, it is recalled that a single fibril of 20 mm. length may contain thousands of such sarcous elements, and that there may be, as Bernstein estimates, over thirty million of such fibrils in a square centimetre of cross section of muscle, it is obvious that the total surface energy set free must be sufficient to account fully for the absolute contractile force of muscle.

The energy thus liberated appears as work, and it is replaced by energy, one may suppose, derived from combustion of certain materials in the doubly refractive discs. In this case the disturbance of surface tension would be primary, while the combustion process would be secondary in the order of time. In support of this explanation may be cited the fact that the current of action in muscle precedes in time the contraction itself; that is, the electrical response of the stimulus occurs in the latent period and immediately before the contraction begins.

It may, however, be postulated, on the other hand, that the chemical changes occur in those parts of the doubly refractive disc immediately adjacent to the singly refractive bands, and as a result the tension of the terminal surfaces is increased, this resulting in the shortening of the longitudinal axis of the sarcous element and the displacement laterally of its contents. This would imply that the energy of muscle contraction comes primarily from that set free in the combustion process and not indirectly as involved in the former explanation.

Whatever may be the cause of the alteration in surface tension there would seem to be no question of the latter. The very alteration in shape of the doubly refractive disc makes it imperative to believe that surface tension is concerned. The redistribution of the potassium which takes place, as described, in the contracting fibrils of the wing muscles of the scavenger beetle can be explained in no other way than through the alteration of surface tension.

In smooth muscle fibre a different structure obtains, although efforts have not been wanting to show that there also prevails a system of fibrils and striation like that in striated fibre, though more obscure or less well defined. The evidence for the existence of fibrils, myofibrils as they are called, seems, on the whole, clear, especially from the results of C. McGill's (79) observations, but it is not so certain that the nodular enlargements occasionally found on these represent a constant or characteristic feature. There is, further, not a united voice about the character of the contraction. According to Heiderich (46), the cross-sectional area of the smooth fibre in contraction is very little, if at all, greater than that of the uncontracted fibre. Meigs (82) also arrived at this conclusion, for he found that, though the contracted fibres have shortened, the cross-sectional area of each is the same, and, in consequence, infers that something in the form of a fluid has passed from the interior of the fibre into the interstitial spaces. McGill, on the other hand, found that the contraction of the fibre is a result of a considerable increase of its cross-sectional area which sweeps as a wave over the length of the fibres from one end to the other, and that this wave only rarely, as in arterial muscle, comprehends the whole length of the fibre. Wherever the contraction wave obtains in the fibre that part is swollen, its cytoplasm stains much more deeply than that of the rest of the fibre, and the portions of the myofibrils in it also stain more deeply and are thicker. Meigs found the contracted part stain deeply, but Henneberg (50) claimed that they stain less than the uncontracted portions of the fibrils.

The author's own observations on carefully hardened and stained preparations of the smooth muscle fibre in the muscularis of the intestine of Necturus and frog agree in the main with those of McGill. The contraction wave does involve a thickening of the fibre, not over the whole of the latter ordinarily, but of part of it, and in this thickened portion the cytoplasm stains much more deeply than does the rest of the fibre. Further, the thickening, which may in diameter be twice that of the relaxed portion, passed gradually into the uncontracted part at either end. There may be several nodes of contraction on a fibre separated by long or short stretches of uncontracted zones.

In the cytoplasm of smooth muscle fibre potassium is present only in the faintest traces, and microchemical tests for chlorides and phosphates show that these also are equally scanty in quantity; consequently, there is very little inorganic material inside the membrane. Outside the membrane and between the fibres potassium salts are very abundant, as the use of the cobalt reagent shows, and the distribution is uniform throughout the interstitial spaces. The salt of potassium most abundant is the chloride, for application of a solution of silver nitrate, containing nitric acid, to the teased-out, fresh material, followed by exposure of the preparation to bright sunlight, gives a marked "reduction" effect everywhere in the spaces between the fibres. The quantity of potassium present is in marked contrast with that which obtains in the interstitial spaces in other tissues, e.g., in those between nerve fibres in a thick nerve. Whether the potassium exists at all in the membrane of the smooth fibres cannot be determined, for, although the cobalt precipitate is found in intimate connection with the membrane, the latter is so thin that no certain conclusion can be drawn on the matter.

In smooth muscle fibre, then, potassium is distributed very differently from what it is in striated fibre, and on first thought this does not appear to offer an explanation that will place the contraction of smooth muscle fibre in line with that of striated fibre, but a closer examination of the facts reveals otherwise. The extended, fusiform character of the fibre indicates that surface tension is greatest on the longitudinal surface and least on the ends. If the tension were uniform over the whole surface of the fibre, the latter would tend to become spherical. A diminution of the tension on the longitudinal surface, or an increase of tension towards and at the ends of the fibre, would have the same effect. A partial diminution of the tension sweeping as a wave over the whole extent of the fibre would account for the thickening of contraction observed. In this respect smooth muscle is like striated muscle, the main difference being that in striated fibre the structure permits a much more rapid transmission, over the whole surface of the fibre, of the alteration in surface tension.

How the diminution of the tension is brought about can only be a matter of conjecture at present. It may be due to a contact difference of potential developed at the membrane-interstitial lymph interface through the arrival there of the nerve impulse which may involve an electrical disturbance. The electrical double layer developed at a point on the membrane would not be restricted there, but would sweep over the whole extent of the surface of the fibre, and as it progressed it would produce a diminution of tension.

What the significance of the condensation of potassium in the interstitial spaces of smooth muscle fibre is cannot be explained at present. Analysis of the sodium and potassium in smooth muscle shows that the latter is more abundant than the former, though the preponderance is not as great as it is in striated fibre.* This leads one to conclude that potassium plays some part in the function of contraction.

It is of special interest to note here that the potassium ions have the highest ionic mobility (transport number) of all the elements of the kationic class, except hydrogen, which are found to occur with living matter. Its value in this respect is half again as great as that of sodium, one-eighth greater than that of calcium and one-seventh greater than that of magnesium. This high migration velocity of the potassium ions indicates that they possess special properties which would make them of special service in rapid changes of surface tension in the case of striated muscle fibre, as assisting in the tendency to uniform distribution of energy throughout the volume of the sarcous element.

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* From unpublished data of the author.

That a solute, e.g., potassium salt, subjected to surface condensation in a system like that represented in a sarcous disc, may be rapidly, even instantaneously, redistributed in consequence of changes in surface tension follows from the observations on the changes of tension in drops of soap solution. By the experiments of Lord Rayleigh (91) with vibrating jets of such a solution it was found that the surface tension of the jet 1/100 of a second after the formation of the surface was near that of pure water, while Lenard (64), by experiments with vibrating drops whose time of formation was greater than 1/4 of a second, found the surface tension of a soap solution of corresponding strength (1:1000) less than half that of pure water and rather near the stationary value of the surface tension of a soap solution. Somewhere then, in the case of soap, in time between 1/100 of a second and 1/4 of a second the molecules of soap have been redistributed so as to adjust the energy uniformly throughout the drop, and, therefore, it is not improbable that potassium salts, and especially potassium chloride, which occur in the doubly refractive bands of striated fibre, would be, as a result of an alteration of surface tension in each sarcous element, very rapidly redistributed throughout the latter, though, perhaps, not so rapidly as the soap molecules throughout the much larger system of a drop or vibrating jet.

It is, however, well to assume that potassium ions have other functions in living matter than the equilibration of energy throughout a system. Loew (69) has specially pointed out that potassium in the condensation processes the synthesis of organic compounds has a catalytic value very different from that of sodium. For example, ethyl aldehyde is condensed with potassium salts to aldol, with sodium salts to crotonic aldehyde (Kopf and Michael). Potassium is, but sodium is not, effective in the condensation of carbon monoxide. When phenol is fused with potassium salts condensation products such as diphenol are produced, but when sodium salts are used the products are dioxybenzol and phloroglucin (Barth). Further, the activity of potassium contrasted with that of sodium is shown in its behaviour with pyrrol. When the metal is brought in contact with pyrrol it combines with the latter at ordinary temperatures, whereas sodium combines with pyrrol only at very high temperatures.

It is, therefore, not improbable that potassium, along with those properties which are associated with its ionic mobility, has a special value in the metabolism of the doubly refractive discs of striated muscle fibre and in the condensation syntheses which characterize the chromatophors of Protophyta (Spyrogyra, Zygnema).

(c) IN SECRETING AND EXCRETING CELLS.

In all secreting and excreting cells in a gland constructed on the tubular plan there must be at least three different values of surface tension. On the outer face, that is, on the cell-lymph interface, the tension must be different from that which obtains where the cell wall is in contact with the other cells of the tubule, and the tension on the cell-cell interface must be different from that which obtains on surface bordering the lumen of the tubule.

This general conclusion, founded on theoretical considerations, has been fortified by direct observations on the distribution of potassium salts in the pancreas and kidney of various vertebrates.

In the pancreas of the rabbit and guinea-pig the author (71) found an extraordinary condensation of potassium salt in the cytoplasm of each cell adjacent to the lumen of the tubule and extending for some distance from this part along the lateral walls of the cell. During all the phases of activity, except possibly that of the so-called "resting stage" of the gland cells, the potassium salts are confined to these surfaces inside the cell. These results were obtained in preparations of the fresh pancreas which had been teased out in the cobalt reagent in which they were allowed to lie for some time, then washed thoroughly in ice-cold water and mounted in a mixture of glycerine and ammonium sulphide.

More recent investigations have confirmed these observations. These investigations were made in a different way. Fresh pancreatic material was cut in a CO_2-freezing microtome, and the thin sections were allowed to fall, while still frozen, into a quantity of the cobalt reagent where they were allowed to lie for some time, ten minutes or so, before they were washed with ice-cold water and mounted in the glycerine-sulphide mixture. Such preparations gave the distribution of potassium, not only inside the cells of the pancreatic tubules, but also on their external surfaces.

In such preparations the potassium was found distributed as described in the case of the teased-out preparations, that is, it was condensed in the cytoplasm on the lumen border and along the lateral walls of the cell even as far as the external surface of the tubule; but one additional fact was revealed, viz., that on the external surface of each tubule there was a very marked condensation of potassium salts. Inside of the cells on the external surface of the tubule no potassium was found. These results were obtained in preparations of the dog, rabbit, guinea-pig, cat, frog and Necturus.

During the last session (1911-12) Dr. R. D. Defries undertook to reinvestigate the relation of potassium salts to secretion in the salivary and pancreatic glands and in the glands of Brunner in the cat, dog, guinea-pig and rabbit, and he has obtained results* in all these which confirm the findings given above. In these glands when in activity, there is, in the cytoplasm of each cell immediately adjacent to the lumen of the secreting tubule, a condensation of potassium salts which is absent during "rest", that is, while the cells are not secreting. In the submaxillary glands this condensation may be quite marked. In the pancreatic cells during activity the condensation frequently extends along the lateral walls, and this is the case also in Brunner's glands. On the external surface of the tubules, in all these glands, there is more or less condensation of potassium, which, however, may be considerably reduced, or even occasionally absent, in the active gland.

These results may be explained only in one way. On the Gibbs-Thomson principle there must be inside the cell a low tension on the cell-lumen interface, a slightly higher tension on the cell-cell interface and a still higher tension at the external surface. What this involves in the way of explaining the phenomena of secretion in the pancreatic cell cannot be discussed, for, beyond the formation of zymogen during the resting condition of the cell, the conversion of the zymogen granules into dissolved material, a part of which is formed to enzymes, and the transport of this material to the lumen of the gland, we know very little, and the processes comprehended in all the stages of this secretory activity are exceedingly difficult to investigate. Nevertheless, the low tension at the lumen border and the high tension at the base of the cell cannot but be a factor, probably a very important factor, in promoting all that activity; in other words, differences in surface tension of a cell are primarily contributory to its secretory activity.

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* These results, it is hoped, will be published shortly.

What part the potassium salts play beyond assisting in equilibrating the energy throughout the cell is also unknown. That they do play a special part follows from the quantity of potassium present. Stoklasa (101) found, as a result of analyses of the dried pancreas of the pig, that it contained 2.08 per cent. of potassium and 0.28 per cent. of sodium, while the two elements in the dried material of ox muscle are, as he determined them by analyses, 1.82 and 0.26 per cent. respectively.* Some of the potassium of the pancreas must belong to that found adsorbed from the lymph on the external surface of the tubule, but this cannot be great unless we suppose that sodium salts are much less adsorbed, a supposition for which we can as yet find no support.

Even in the ash of the saliva potassium exceeds the sodium, for Hammerbacher (45) found in his analyses the two elements to be respectively 37.4 and 7.0 per cent., while Jacobi (53) obtained in two series of analyses 35.69 and 35.88 per cent. for potassium and 21.61 and 32.91 per cent. for sodium.

The occurrence of a surface condensation of potassium outside the tubule on the base of each cell is an indication that, as compared with that of lymph, the surface tension of the cell-lymph interface is lower than it is on the surface of a connective tissue element where there is very little adsorption of potassium. If potassium salts constitute an important factor in secretion in the pancreas, then any influence that decreases still more the surface tension of the lymph, or increases the surface tension at the base of each pancreatic cell, would promote a greater adsorption there of potassium salts. Have we in this increase of surface tension an explanation of the action of secretin, or of the effects of stimulation of the vagus, in the experiments of Pavlov, on the pancreatic cells?

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* Stoklasa gave the values in K_2O and Na_2O.

In the kidney of vertebrates the part played by surface tension is much more striking and more readily explainable. Two years ago the author (72) described the results of an investigation which he carried out on the microchemical localization of the potassium in the renal cells of the frog. In this animal under ordinary conditions the renal cells were found to be active in the elimination of potassium salts from the blood, and, therefore, it was not possible to determine readily whether differences of surface tension obtained in them. Under certain conditions, however, these differences were demonstrated to occur. In the blood of frogs kept in the laboratory tanks throughout the winter season, the salts, because of the long period of inanition, are reduced to almost hypotonic concentration, and, in consequence, the amount of potassium in their renal cells is greatly reduced. Into the dorsal lymph sacs of some winter frogs a few cubic centimetres of a decinormal potassium chloride solution was injected, and after twenty minutes the animals were killed and the kidneys removed. Sections made immediately from these with the CO_2-freezing microtome, dropped while frozen into the cobalt reagent for a few minutes, then washed carefully in ice-cold water and mounted in a mixture of glycerine and ammonium sulphide, revealed a condensation of potassium immediately adjacent to the lumen in the cytoplasm of the cells of certain of the tubules. In such cells the potassium of the potassium chloride injected was being excreted, and the condensation of the element near the lumen was regarded as evidence that the surface tension was less there than at the other extremity of the cell.

Since then Mr. C. P. Brown has carried out observations along this line under the author's supervision, and the results he has obtained corroborate, on the whole, the views advanced two years ago.* He employed in his investigations the kidney of the frog, Necturus, cat, dog, rabbit and guinea-pig, and the methods which he used were those employed earlier by the author. Care was taken to use only material fresh from the normal animal, which was at once on removal sectioned in the CO_2-freezing microtome, and the sections placed, while still frozen, in the cobalt reagent for a few minutes. The reason for the exercise of this caution was to prevent the redistribution of the salts which might occur on thawing before the reagent penetrated the tissue. The sections were on removal from the reagent carefully washed in ice-cold water and mounted in the glycerine-sulphide mixture. The best sections, on the whole, were those of a thickness of 10μ.

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* The results of Mr. Brown's investigations are in the course of publication.

In such preparations Mr. Brown found striking indications of the surface condensation of potassium. In the winter frog wherever it was found, the condensation was on the outside of the tubules and in the cytoplasm of the renal cells immediately adjacent to the lumen of the tubule. With the exception here and there of a slight deposit of potassium along the lateral walls of the cells, the rest of the cytoplasm was free from the elements. In convoluted tubules of the cat, rabbit and guinea-pig, similar results were obtained, but the most striking evidence of surface condensation was observed in the kidney of the dog. In this animal the great majority of the convoluted tubules were in this way contrasted with the other tubules, which only rarely showed any evidence of surface condensation. An illustration of the way in which the convoluted tubules develop surface condensation of potassium is seen in Fig. 15. Here the potassium is densely collected on the outside of the tubule, that is, on the cell-lymph interface, and also more densely in the cytoplasm immediately adjacent to the lumen. Sometimes a portion of a convoluted tubule would for some extent of its length give no evidence of condensation either within or without. Again, on the external surface of one or more cells in a transverse section of a tubule, there would be no condensation, but in such cells there was wanting also frequently a condensation at the lumen.

The significance of these facts is not far to seek. The condensation in the cytoplasm next to the lumen of the tubule is an indication that the surface tension of the renal cells is lowest on the border of the lumen. In this condensation other salts must participate, and perhaps, also, urea and other organic, excretory products, all of which would be as strikingly demonstrated as are the potassium salts, had we delicate, microchemical reactions for them. Now, along the cavity of the lumen passes the dilute glomerular secretion with, probably, a high surface tension, and, in consequence, at the interface it forms with the surfaces of the cells of the tubules, its surface tension is probably higher than that of the cell surfaces bordering the lumen. This would involve a diffusion, chiefly from the constituents of the surface condensation in the cytoplasm, into the glomerular secretion, which, as it passes down the length of the lumen, becomes more and more concentrated until, finally, it reaches those parts of the renal tubule in whose cells there is no surface condensation. Whether there is a diffusion of the glomerular secretion into the cells possessing a surface condensation cannot be determined, but it is likely that there is, as it is impossible to conceive that diffusion of the salts into the lumen could otherwise take place.

If, however, this diffusion into the cells occurs, it would tend, it may be supposed, to raise the surface tension of the lumen wall of the cell, and then the surface condensation would disappear. This would, on the explanation given, involve a cessation of excretory activity on that part of the tubule.

How the low tension on the lumen side of the renal cell is maintained cannot be determined, but some factors in this process may be suggested. The condensation probably exceeds the value given in Gibbs' equation. Indeed, the fact that practically no potassium is present in the cytoplasm of those cells in which there is a marked condensation of potassium next to the lumen is strong evidence that a much greater concentration of the potassium occurs there than the equation would imply. In Lewis' determinations the potassium adsorbed on the surface of oil drops in a solution of potassium chloride was thirty times the amount calculated from Gibbs' equation. It is therefore not unreasonable to suppose that adsorption in excess of the calculated value may obtain in the renal cells. This excessive concentration would, as explained, lead to the formation of urine of high concentration, a concentration in salts and metabolites ordinarily far in excess of that of the blood plasma. Such a concentration involves expenditure of energy, and the energy so expended is surface energy. To furnish this energy the metabolism of the cell must be so controlled that low surface tension on its lumen border may be maintained, or that a higher one at the external surface of the cell should be developed and continued. The energy involved here must come from the combustion of material in the cell. On this point there are some decisive data. From the investigations of Barcroft and Brodie (3, 4) it is known that the kidney during diuresis absorbs a very large quantity of oxygen. For instance, in one of their series of experiments the kidneys in a dog, during diuresis, absorbed 11 per cent. of the total oxygen absorbed by the body of the animal during that period, although they constituted less than 1 per cent. of the total body weight, and in all such experiments the oxygen absorbed by these organs in diuresis much exceeded that absorbed per gram weight by the body generally. These authors are led to conclude that a copious flow of urine, whatever its concentration may be, is accompanied by intense chemical activity in the kidney. Assuming that the oxygen absorbed is used up in the oxidation of a proteid, and estimating the energy expended in producing the urines of the concentration they obtained, they calculate that on the average only 1/220 of the energy liberated by the oxidation is represented by the concentration of the urine. That the oxidation is completed there, and also that the energy arising from the oxidation is expended there, appear to be shown by the fact that the sum of the quantities of oxygen taken in by the kidney during the periods it was under observation was almost exactly equal to the sum of the quantities of carbon dioxide set free.

But why the large amount expended? It is obvious that a very considerable portion of it is to be accounted for on the principle of the "factor of safety" which, as Meltzer has pointed out, prevails in other organs of the body, but there remains an amount of energy the expenditure of which cannot thus be explained, unless it be that in the kidney, of all the organs of the body, the "factor of safety" is given an extraordinary magnitude. We may, however, account for it by supposing that whether the glomerular secretion is or is not flowing down the lumina of the tubules, the difference in surface tension in the cells of the convoluted tubules must be continuously maintained, and that what this means in the way of expenditure of energy may be very great.

What part in this maintenance of difference in surface tension is played by the potassium present is obscure, but that the element does play a part is indicated by the qu[illegible] present in the kidney. Mr. C. P. Brown has dete[illegible] the quantities of sodium and potassium in the kidney of the frog to be 0.188 and 0.1905 per cent respectively, and in the kidney of the dog the percentages were 0.1777 and 0.2355. Here, indeed, we have a high concentration of potassium which cannot be explained by supposing that organs as analysed contained a large quantity of blood. The sodium could be accounted for by supposing that a large portion of it as chloride is derived from the lymph, which, however, is poor in potassium. It may be that the quantity of potassium present in the kidney is only a specific instance of a general fact, namely, that in all living matter potassium is more abundant than sodium.

In spite of the obscurity that affects a number of points in the excretory function of the kidney, there are the facts described, which indicate what are the main forces involved in the exercise of that excretory function. There is, first of all, the condensation on the exterior surface of the convoluted tubules, this condensation involving not only potassium but probably, also, all the other solutes of the blood plasma and lymph, though not in concentrations corresponding to those obtaining in the latter fluids. The concentration of a solute, like potassium salt, in this condensation layer would then bear no direct relation to its concentration in the lymph and plasma. Now, the close association of such a condensation with the surface of the renal cells would permit the latter to receive by diffusion some of the condensed solutes. Owing to the low tension on the lumen surfaces of the cells acting through the Gibbs-Thomson law, the solutes absorbed would be swept through the cell to the surface of low tension where they would undergo surface condensation. This condensation may far exceed the concentration on the lymph-cell interface, but this would depend on the rate of flow down the tubule and on extent of the metabolic processes in the cell which bring about the differences in surface tension.

Differences in surface tension appear to be a factor in intestinal absorption also. The facts in regard to this have not been specially investigated, but enough are known to make out a prima facie case in support of this thesis. In the author's observations (70) on the absorption of iron salts in the intestine of the guinea-pig, it was found not infrequently that after "peptonate" of iron had been administered with the food of the animal the iron demonstrated was condensed at the basal surfaces of the epithelial cells of the villi. When also potassium salts are being absorbed by these cells it is rare to find potassium in the cytoplasm adjacent to their free borders, although it is condensed along the cell-cell interfaces and in the cytoplasm next to the basal surfaces of the cell. In the absorption of fats the epithelial cells of the intestine, as a rule, show a greater condensation of fats in the cytoplasm at the basal ends of the cells than elsewhere in the epithelium.

These facts permit us to suggest that in the epithelial cells of the intestine the highest surface tension is on the free border and the lowest at the basal ends of the cells. If this should ultimately prove correct, then the process of absorption would be explained by the application of the Gibbs-Thomson principle. There would be a surface condensation of solutes in the intestinal fluids on the external free surface of each cell, and whatever diffused into the cells would be swept through their cytoplasm to the surface of low tension on the basal border on which the lymph of the cell-lymph interface has a surface tension which is probably different (higher?) from tha of the basal surface of the cell.

If this view of absorption is correct, then there is no fundamental difference between absorption, on the one hand, and secretion and excretion, on the other. These three functions would then be explained as due to the capacity which the cells concerned have of maintaining differences of surface tension on their two active cell surfaces, and while these differences would be maintained the Gibbs-Thomson principle would continuously operate.

(*d*) IN NERVE CELLS AND NERVE FIBRES.

When a nerve is cut there occur the well-known phenomena of degeneration in the fibres on the distal side of the section. On the central side changes are found also in the fibres, but they are chiefly of the reparative type. The soft colloidal substance of each axon flows out, as it were, beyond the cut end, and this movement, comparable to the extension movement of amœboid organisms, continues, either until the outflowing material enters and occupies a neurilemmal tube of the degenerated distal strand of fibres, or, failing that achievement, ultimately the nerve cell from which the colloidal outflow primarily proceeds itself degenerates.

The whole of the process involved in the regeneration of nerve fibres suggests strikingly that surface tension is primarily involved. Indeed, the development in the first place of the axon from the embryonic nerve cell is, it must be inferred, due to a high surface tension on the latter, accompanied by a low tension at the terminal point of the extending axon. The fact that the axon is maintained throughout the life of the normal nerve cell as an extension of the cytoplasm of the latter is also an indication of the prevalence of a constant difference between the surface tension of the surface of the cell body and that of the surface of the axon.

That this is not wholly a-prioristic is shown by the results of microchemical investigation of the nerve cell and nerve fibres. The author's observations published seven years ago showed that potassium is abundant along the course of the axon and apparently on its exterior surface, while it is present only in traces in the nerve cell itself. In the latter chlorides are present only in traces, and, therefore, sodium, if present, is there in more minute quantities, while chlorides are abundant along the course of the axon. Macdonald (76) also found potassium in the nerve fibre, and his observations in the main confirmed the author's. He held that the element is in a "masked" condition in the axon, and that it is demonstrable only in the parts of the axon which have undergone injury. The potassium set free diffuses from an injured point into the adjacent portions of the nerve fibre, and this phenomenon is accompanied by an electrical phenomenon, the injury current, which, traversing the fibre, polarizes it and gives rise to the appearance of a new mass of potassium solution, accompanied by appearances characteristic of coagulation at the cathodal region.

The author has more recently reinvestigated the question, and as a result finds that when cross sections of a fresh nerve made with the CO_2-freezing microtome are dropped, while still frozen, into the cobalt reagent, and later treated to bring out the potassium reaction, the latter is found in the myelin sheath and between the axon and the sheath (Fig. 18). In the latter case the potassium is not abundant, but it must be noted that the section itself is only about 10μ thick, and that the extent of the axon included is only a little more than the diameter of mammalian red blood corpuscle. That in nerve fibres teased out in the cobalt reagent the quantity of potassium demonstrated at any point should appear more abundant is not surprising, for the reagent only slowly penetrates the fibre at the nodes of Ranvier, and this causes currents of diffusion to set up within the medullary sheath, with the result that inequalities in the distribution of potassium along the surface of the axon occur. This may lead to considerable accumulations of the cobalt potassium salt at a point (Fig. 17) which, if their mode of production is not recognized, may give confused ideas regarding the distribution and amount of potassium along the course of an axon. The quantities of varying magnitude of the potassium involved, if uniformly distributed along the fibre, would not be more abundant than is the potassium revealed in the 10μ-length pieces of the axons in the cross sections of the nerve made with the freezing method.

The special point to note, however, in these sections, as in the teased-out preparations, is the occurrence of the potassium salts, as indicated, between the medullary sheath and the axon. As Macdonald has pointed out, the transverse diameters of the axons in these preparations are nearly always less than those of the fresh fibres, and, consequently, the free space between the medulla and the axon shown in the cobalt preparations is an artefact. One must conclude, in consequence, that the potassium revealed in this free space must have been derived from the shrunken axon, whether from its surface or from immediately inside its surface as the author holds, or from the more central as well as from the peripheral substance of the axon in cross section, as Macdonald postulates.

Macdonald's view that the potassium in nerve fibre in the uninjured condition is in a "masked" condition the author finds difficult to accept. Monovalent kationic elements are not known to enter into the "masked" condition. Monovalent anionic elements can do so, as, for example, chlorine in the case of chloroform. Divalent and trivalent kationic elements are known to enter into the "masked" condition in certain of their organic compounds. Potassium, however, when it displaces hydrogen in an alkyl or aryl group, is quickly removed from the compound when the latter is treated with water. An illustration of this is seen in potassium pyrrol, which at once decomposes when brought into contact with water. The cobalt reagent containing a strong concentration of nitrous acid cannot be less effective in this respect than water, and, consequently, any organic compounds of potassium in the axon would be readily revealed. Moreover, the prevalence of haloid chlorine in considerable abundance in the axon, as revealed by treatment of nerve fibre with silver nitrate in a dilute solution of nitric acid, followed by exposure to bright sunlight, shows that there must be some kationic element present to form the chloride compound, and if this element is potassium, some of it cannot be in a "masked" condition.

That potassium is specially abundant in the axons of nerve fibres seems to be suggested by the analyses of Alcock and Lynch (1), who have found that in medullated nerve fibres the percentage of potassium is 0.284, while in connective tissue it is 0.043, and they conclude from their determinations that in the axons it cannot exceed 1.17 while the chlorine cannot exceed 0.722. It would, therefore, appear that a large part of the potassium in nerve fibre is combined with some other anion than chlorine.

It is not a matter of moment at present whether the potassium of the axons of nerve fibres is immediately inside the surfaces of the axons, as the author holds, or uniformly distributed throughout the substances of the axon, as Macdonald claims. The point of special importance to note is that potassium is specially abundant in nerve fibres. This is emphasized not only by Alcock and Lynch's determinations, but also by those of Geoghegan (41) and Mr. Allman Fletcher. In Geoghegan's analyses the potassium in the human brain exceeded the sodium by fifty per cent. at least, and in one case by nearly one hundred per cent. Mr. Fletcher found that in the cerebrum of the sheep the potassium is 0.331 per cent. and in proportion to the sodium as 100 is to 57.4.* It is thus evident that in nervous tissue potassium far exceeds sodium in amount.

Potassium, abundant though it apparently is along the course of the axon, does not occur inside the nerve cells themselves, or if it does occur in them, it is only in quantities so minute as to be beyond the capacity of the cobalt reagent to demonstrate it. Hence, the potassium shown to be so large in amount in the cerebrum must be present chiefly in nerve fibres and in structures outside the nerve cells themselves. That the amount external to the nerve cells is great is shown by treating frozen sections of fresh ganglia, preferably the Gasserian, appropriately with the cobalt reagent to demonstrate the potassium present. In such preparations there is found a very considerable condensation of the element on the surface of each nerve cell. This indicates that the surface tension of the lymph at the lymph-nerve cell interface is low, and, in consequence, other solutes than potassium salts are condensed there also, but Geoghegan's and Fletcher's determinations would seem to suggest that perhaps potassium is more abundant than sodium in that condensation.

Now, the condensation of potassium on the surface of the body of a nerve cell, the absence of potassium in its cytoplasm, and the occurrence of potassium salts in apparently a very considerable concentration along the course of the axon, whether within its medulla-axon interface or distributed, as Macdonald holds, uniformly throughout the axon, is extremely significant. It is the effect of the action, in nerve cells and their prolongations, of the Gibbs-Thomson principle of surface condensation due to differences of surface tension on the surfaces of the nerve cell and of its axon. We have here, therefore, a confirmation of the generalization advanced above, that the permanent maintenance by the nerve cell of an axon is due to the maintenance of a difference in surface tension between the body of the nerve cell, on the one hand, and the axon, on the other. Just as the soft colloidal substance of the axon in the regenerating nerve fibre flows out of and beyond the cut end of the latter, because of this difference of surface tension, so any potassium salt that may be absorbed by the cell body from the potassium salts condensed on its surface is swept, through the action of the Gibbs-Thomson principle, into the region where the lowest tension prevails, that is, into the axon, even to its extreme end.

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* The determinations were made in the Biochemical Laboratory of the University of Toronto. The results will be published shortly.

It is this which makes intelligible why the nerve cell is free from potassium. Otherwise it would have to be supposed that the surface of the nerve cell is impermeable to potassium salts, while the surface of the axon is permeable. If this were the correct explanation, it would indeed be difficult to understand how the potassium could get through the medullary sheath to the axon in such a quantity as has been demonstrated to be present there, as it is only very slightly condensed on the neurilemma-lymph interface of the nerve fibre. The condensation of potassium salts in the axon is, then, the effect of the constant action in the nerve cell of the Gibbs-Thomson principle.

The conclusions that follow from this are of special interest. We know that electrical polarization of ever so slight a character occurring at a point on the surface of a drop of mercury, water, or some other fluid, lowers correspondingly the surface tension at that point, and if solutes are present in the drop, these, in consequence of the alteration of surface tension, are redistributed so rapidly that a condition of complete equilibrium may be attained in less than a small fraction of a second. Lenard (64), it may be pointed out once more, found in drops of soap solution (1:1000) 1/4 of a second after they were formed that the tension had a value of less than half that of pure water and rather near the stationary value of such a soap solution, while Lord Rayleigh (91) found that in vibrating jets the surface tension of a solution of soap of like concentration 1/100 of a second after the formation of the surface, was found to be near that of pure water. This makes it evident that the distribution of solutes is rapidly affected by changes in surface tension. In a nerve cell, which may be considered to be of a semi-viscid, semi-fluid character, any temporary alteration of surface tension ever so slight will instantaneously and correspondingly affect the distribution of the salts condensed along the course of the axon. If the alteration of surface tension exists for only a minute fraction, e.g., 1/100 of a second, the redistribution of the salts in the axon, though initiated, would involve only an infinitesimal amount of shifting along the axon, but an immediate replacement would occur on the re-establishment, in the next 1/100 of a second, of the previous value of the surface tension.

Now, each alteration, however slight, in the distribution of such salts would be a progressive one along the course of the axon, and as the redistribution must begin at the central end of the axon, it would initiate there a change of electrical potential which would be transmitted, with the displacement of the potassium ions at each point in succession, along the axon to its termination. This change of electrical potential as it progresses along the axons would constitute the current of action, and it would occur as often as a change of tension could occur on the surface of the nerve cell.

What a nerve impulse fundamentally involves in the axon is not yet fully known, but it is always accompanied by, if not constituted of, the change of electrical potential which is known as the nerve current of action, and which is as rapidly transmitted as is the nerve impulse itself. It may, in the final analysis, be found that the current of action itself constitutes the essential part of the nerve impulse. As postulated in the discussion on the effect of surface tension in muscle fibrils, the arrival at the surface of a sarcous disc of this current of action would bring about there electrical polarization and thus alter the surface tension of the disc, developing, in consequence, contraction or shortening of the disc. Here the current of action would perform all the functions that a "nerve impulse" is supposed to perform. So in the nervous system the transmission of a nerve impulse from one part to another could be effected through the change of electrical potential transmitted along an axon through its synaptic terminals to the surface of another nerve cell, to produce there a contact difference of potential and thus alter its surface tension. The axon of this nerve cell would thus experience a momentary and slight shifting in position of its potassium salts, and in it would thus arise a corresponding current of action which would proceed along the course of the axon to its termination, whether in the immediate vicinity of another nerve cell, or in a gland, or in a motor structure. The arrival of the current of action at any one of these terminal points would affect the surface tension there, and call forth effects commensurate with the resulting change in surface tension.

That the nerve impulse is nothing more than the current of action would appear to follow from what we know of the effect of stimulation of a cut nerve, e.g., the ischiadic in the frog. Here the axon is cut off from the nerve cell itself, and, in consequence, the surface tension of the axon must, for a time, remain practically uniform if the physical conditions about the cut end are not immediately altered. If now electrodes are applied and a slight electric shock administered, the surface tension in the region immediately affected by the current should be lowered, and there should result a slight shifting of potassium salts, which should sweep in a wave-like fashion over the axon to its terminals, producing the current of action and causing contraction of the muscles supplied by the nerve. The application of chemicals or of heat gives rise to a current of action, and the muscle contracts. This also may be explained by the effect that these agents have on the surface tension at the point where they are applied. Suddenly effected deformations of the axons would also alter surface tension, and one may thus account for the nerve impulses generated by pinching or striking a nerve.

When a constant current, instead of an interrupted one, is used the shifting of the potassium salts to re-establish equilibrium disturbed by the alteration in surface tension should develop rapidly, if not immediately, after the closure of the circuit, and thereafter, so long as the current passes, no further current of action would be produced; but when the circuit is opened then the surface tension of the part of the nerve in the circuit would tend to return to its original value, the molecules of the potassium salts would tend to shift back to their former position, a current of action, simple or composite in character, would arise, and the muscle would contract once, or, as in Ritter's opening tetanus, several times.

It is not necessary to elaborate this view extensively. It suffices, perhaps, to say that alterations of surface tension in nerve structures account also for the phenomena of electrotonus, the velocity of the nerve impulse and the effects of heat and cold, but, above all, we can thus explain anæsthesia and narcotism. Chloroform, ether, alcohol and chloral lower surface tension in aqueous solutions, in blood plasma and lymph, and, in all probability also, the surface tension of all cells, but especially of the nerve cells. This would make them incapable of receiving or transmitting a nerve "impulse" whether of a motor or of a sensory character.

Sensation, then, is fundamentally and primarily a result of alteration of surface tension in nerve cells and their processes. Whether all the psychic functions may be due to the play of the force of surface tension in the nervous system is a more difficult question. Memory may arise from the adjustment of the surface tensions of the cells in the association and other centres of the cerebral cortex, but one must not leave out of account the thermodynamic and chemodynamic forces, and, before all else, the probably enormous intrinsic pressure in the interior of the nerve cells.

These forces must play their parts in the psychic processes. They cannot, however, be supreme, for, as pointed out in Section II in the foregoing pages, surface tension controls the distribution of the solutes in a fluid, and the distribution of the solutes influences also its thermodynamic and chemodynamic forces. Therefore, in a nerve cell the thermodynamic and chemodynamic processes and the intrinsic pressure may reasonably be supposed to be subordinate to the force of surface tension through which the body of the nerve cell can control the physical and chemical properties of even the most distant extremities of its own extensions, whether they are dendrites or axons.

V.—LITERATURE.

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VI.—EXPLANATION OF FIGURES.

NOTE.—In all the Figures the distribution of potassium, as revealed by the cobalt hexanitrite method, is represented in black shading.

Fig. 1. Cell of Spirogyra sp., showing condensation of potassium on the chromatophor. × 500.

Fig. 2. Two threads of Spirogyra sp. in conjugation with surface condensation of potassium at the tips of the outgrowths developed to produce zygospores. × 450.

Fig. 3. A thread of Pleurocarpus sp. preparing for conjugation. At the elbow of the cell where the conjugation with another cell is to occur the potassium is densely concentrated. × 560.

Fig. 4. Conjugation in Mesocarpus (?) sp. × 560.

Fig. 5. Ulothrix sp. × 500.

Fig. 6. Confervoid accompanying fresh cultures of Zygnema, showing condensation of potassium especially at ends of cell. × 500.

Fig. 7. Germinating Spores of Equisetum arvense. *a*, earlier; *b*, later stage. × 250.

Fig. 8. Cell from the mesophyllous layer of the Easter Lily. × 680.

Fig. 9. Showing "guard cells" of a stoma of Tulipa sp. × 1000.

Fig. 10. Spermatid from guinea-pig, showing potassium condensed at the point of the cell where the tail of the spermatozoon is to develop. × 800.

Fig. 11. Wing muscle of Æschna. Drawn by Miss M. L. Menten. × 1000

Fig. 12. Wing muscle fibres from scavenger beetle, showing difference in the distribution of potassium in the anisotropic substance. *a*, uncontracted, *b* contracted. × 1380.

Fig. 13. Smooth muscle fibres, frog's bladder. The potassium is distributed between the fibres. *a*, a superficial view of a portion of a fibre. × 680.

Fig. 14. Cross section of an acinus of the pancreas of a guinea-pig, showing surface condensation of potassium on the lumen border of the cells. × 1380.

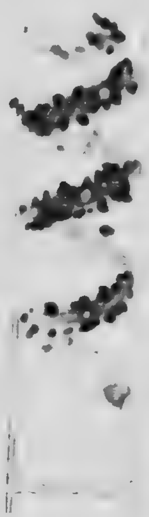
Fig. 15. Cross section of convoluted renal tube in dog, showing surface condensation outside the tubules and on the wall of each renal cell adjacent to the lumen. × 800.

Fig. 16. Cross section of renal tubule in dog, showing condensation of potassium on the lumen surface of each cell while certain portions of the external surface of the tubule are free from any condensation. × 800.

Fig. 17. Nerve fibre, ischiadic, frog, showing potassium on the surface of the axon in the neighbourhood of a node of Ranvier. × 680.

Fig. 18. Cross sections of nerve fibres in Gasserian ganglion of dog, showing potassium in the medullary sheaths and on the surface of the axon. × 800.

Fig. 19. A nerve cell from Gasserian ganglion of dog, showing surface condensation of potassium. × 800.



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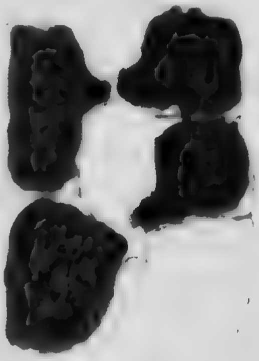

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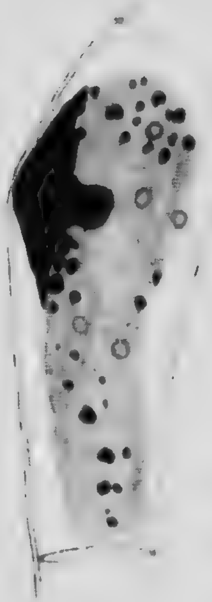

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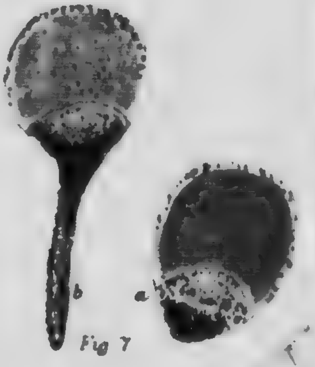

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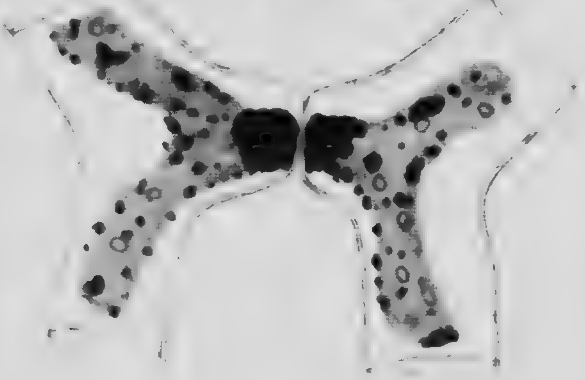


Fig 4

Fig 5.

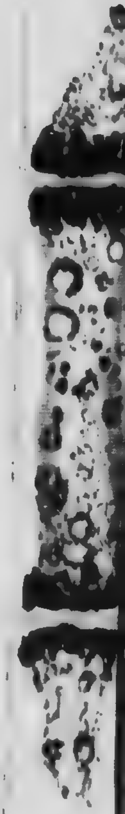
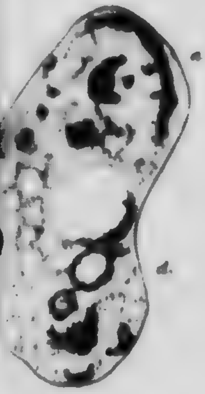


Fig 6

Fig

Plate I



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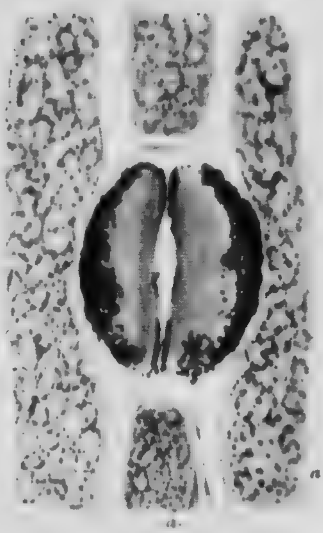

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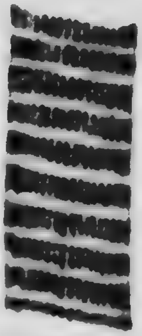
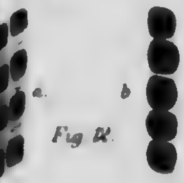


Fig 11



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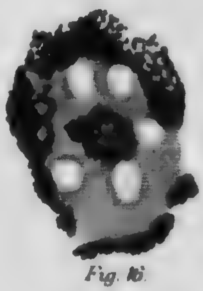

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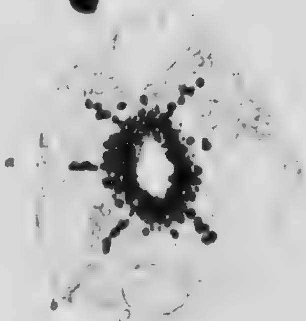

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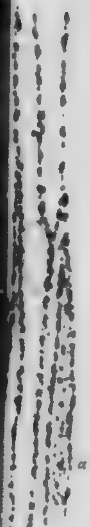

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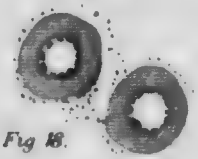

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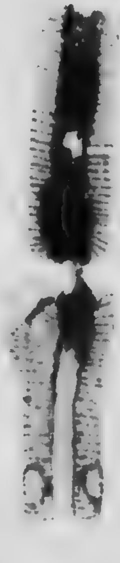
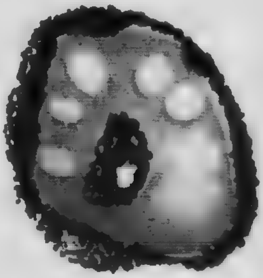


Fig 17



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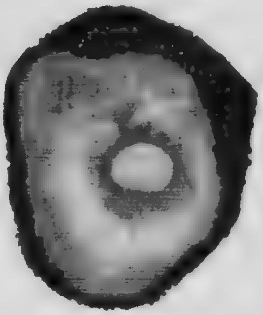
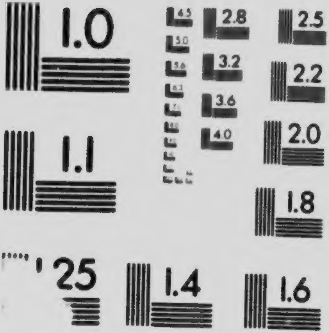


Fig 19

[illegible]

MICROCOPY RESOLUTION TEST CHART

(ANSI and ISO TEST CHART No. 2)



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